Childhood dairy intake and adult cancer risk: 65-y follow-up of the Boyd Orr cohort

Jolieke C van der Pols, Chris Bain, David Gunnell, George Davey Smith, Clare Frobisher, and Richard M Martin

ABSTRACT
Background: Dairy consumption affects biological pathways associated with carcinogenesis. Evidence for a link between cancer risk and dairy consumption in adulthood is increasing, but associations with childhood dairy consumption have not been studied adequately.

Objective: We investigated whether dairy consumption in childhood is associated with cancer incidence and mortality in adulthood.

Design: From 1937 through 1939, some 4999 children living in England and Scotland participated in a study of family food consumption, assessed from 7-d household food inventories. The National Health Service central register was used to ascertain cancer registrations and deaths between 1948 and 2005 in the 4383 traced cohort members. Per capita household intake estimates for dairy products and calcium were used as proxy for individual intake.

Results: During the follow-up period, 770 cancer registrations or cancer deaths occurred. High childhood total dairy intake was associated with a near-tripling in the odds of colorectal cancer (multivariate odds ratio: 2.90 (95% CI: 1.26, 6.65); 2-sided P for trend = 0.005) compared with low intake, independent of meat, fruit, and vegetable intakes and socioeconomic indicators. Milk intake showed a similar association with colorectal cancer risk. High milk intake was weakly inversely associated with prostate cancer risk (P for trend = 0.11). Childhood dairy intake was not associated with breast and stomach cancer risk; a positive association with lung cancer risk was confounded by smoking behavior during adulthood.

Conclusions: A family diet rich in dairy products during childhood is associated with a greater risk of colorectal cancer in adulthood. Confirmation of possible underlying biological mechanisms is needed.


KEY WORDS Dairy products, neoplasms, life-course analysis, incidence, mortality, United Kingdom

INTRODUCTION
The exact relation between dairy consumption and cancer risk remains unclear and is likely to vary by cancer type and the timing of exposure. The main biological pathways through which a person’s dairy intake is suspected to modify cancer risk include greater circulation of insulin-like growth factor I (IGF-I) (1, 2), modification of vitamin D status (3, 4), a greater intake of conjugated linolenic acid (5, 6), and exposure to contaminants such as polychlorinated biphenyls (7–9).

IGF-I plays a central role in the regulation of prenatal and postnatal growth, but it also exerts a growth-promoting effect in adulthood through low apoptosis, high cell proliferation, and angiogenesis (10). High concentrations of IGF-I are associated with a greater risk of prostate, colorectal, and premenopausal breast cancer (11, 12). Milk intake is positively associated with plasma IGF-I concentrations in cross-sectional (13–16) and experimental (17) studies of adults and children (2, 18). In contrast, inverse associations between milk intake in childhood and IGF-I concentrations in adulthood have been reported in a randomized controlled trial of prenatal and postnatal milk supplementation (19). Similar findings have been reported in a recent analysis of the Boyd Orr cohort (20). A long-term programming effect of early diet on the IGF-I axis and cancer risk has been proposed (21, 22).

It has been proposed that high calcium intakes, including calcium of dairy origin, may increase prostate cancer risk by lowering circulating 1,25-dihydroxyvitamin D [1,25(OH)2D] (4, 23, 24), which regulates growth and differentiation in multiple normal and malignant cell types (25). In contrast, dietary calcium may help prevent colorectal cancer through the binding of bile acids in the small intestine and its involvement in the vitamin D pathway (26).

The intake of dairy products thus may affect a mixture of pathways associated with carcinogenesis, and the existence of an early-life programming effect of dairy consumption remains largely unknown. To date, most studies of dairy consumption and cancer risk have been based on adult dairy intake estimates. A comprehensive review concluded that adult milk consumption does not appear to have a strong association with breast cancer risk (27), but a study in Norwegian women showed that the combination of high childhood and high adult milk consumption is a significant predictor of lower breast cancer risk (28). Two US studies also found that milk intake in childhood (29) and milk-fat...
consumption in adolescence (30) were associated with a lower risk of breast cancer, in which both the calcium-vitamin D pathway (31) and the IGF axis, through their effect on breast density (32), were suspected to play a role. Adult dairy consumption has fairly consistently been found to have a small positive association with prostate cancer risk (23, 33) and to be inversely associated with colorectal cancer risk (34–37), but the effect of childhood exposure to dairy products on cancer risk has not been evaluated.

SUBJECTS AND METHODS

The Boyd Orr Cohort

The establishment of the Boyd Orr cohort has been described in detail elsewhere (38). 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-World War II (preshi) Great Britain (39). The survey was carried out from 1937 through 1939 in 1343 families, mainly working-class, who were living in 16 rural and urban areas of England and Scotland. Detailed measurements were made of household diet (see below) and of the health, growth, and living conditions of the children in the households. The name, age, and address of the children (mean age: 8 y; interquartile range: 4–11 y) in the surveyed families were obtained from the original records and used to trace them through the National Health Service Central Register (NHSCR).

Of the 4999 children identified, 4383 (87.7%) have been successfully traced and are included in this analysis; of the remaining 616 participants, 424 could not be identified through the NHSCR, 171 were censored before 1948, and 21 were identified but had been lost to follow-up by the NHSCR. As a result of further searches of archived records, contacts with surviving study members, and additional notifications from the NHSCR, the trace rate has increased slightly since earlier publications. The representativeness of those traced was described previously (38). Traced survey participants were almost 1 y younger than their untraced counterparts (P < 0.0001) but did not differ in terms of childhood energy intake, food expenditure, or socioeconomic status (SES). The NHSCR was used to follow up survey members for mortality and cancer registration (38). Cause of death is ascertained from death certificates; partly with the use of cancer registrations, the cause of death was classified according to the International Classification of Diseases, 9th (ICD-9) and 10th Revisions (ICD-10).

This analysis is based on traced cohort members who were resident in Great Britain on 1 January 1948 and on cancer deaths and registrations 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; 9 traced participants were excluded because some of their dietary data were missing.

Ethical approval for the revitalization of the Boyd Orr Study was provided by the local Research Ethics Committee of the United Bristol Healthcare Trust.

Dietary assessment

Dietary data in the original Carnegie survey were obtained by using a 7-d household inventory method (39, 40). 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 a second inventory was carried out at the end of the survey period. Data from the diaries were then transcribed onto separate summary sheets for each household. Reanalysis of the food records was necessary to include nutrients not measured in the original study and to make use of advances in analytic techniques for foods whose composition is unlikely to have changed from the 1930s to today. Recording of the foods for the present study was carried out by using a diet-in, data-out program (DIDO software; Medical Research Council Human Nutrition Research Center, Cambridge, United Kingdom) (41). Total fruit and vegetable (excluding potato) consumption was reanalyzed with the use of programs based on McCance and Widdowson’s The Composition of Foods (42) and supplements to that publication. Prewar food tables were used to adapt the database if the composition of 1930s foods was very different from that of foods today, or if there was no modern-day equivalent. Per capita food and nutrient intakes 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), infant formulas, cream, cheese, ice creams, and milk puddings.

Statistical analysis

A composite outcome was derived from the presence of a cancer code anywhere on the death certificate or from the first cancer that was registered. Cancer sites were defined as all cancers—ie, all malignant neoplasms (ICD-9 codes: 140.0–208.9; ICD-10 code: C0–C97), breast cancer (ICD-9 codes: 174.0–174.9; ICD-10 codes: C50–C509), lung cancer (ICD-9 codes: 162.0–162.9; ICD-10 codes: C33–C349), colorectal cancer (ICD-9 codes: 153.0–154.9, excluding 154.2 and 154.3; ICD-10 codes: C18–C20), prostate cancer (ICD-9 code: 185; ICD-10 code: C61), and stomach cancer (ICD-9 code: 151; ICD-10 code: C16).

Intake estimates of total dairy products, dairy subgroups (ie, milk, cheese, cream, milk pudding, and ice cream), and calcium were categorized into 4 equal groups according to their distribution in the study population. Odds ratios (ORs) for each cancer type and all cancer types combined were calculated by comparing each of the higher exposure groups with the lowest group by logistic regression analysis. To estimate associations between dairy products and cancer risk, we used logistic regression models, rather than Cox or Poisson regression, because the timings of cancer registrations and death in relation to cancer diagnosis are different, and thus the timings of the composite outcomes are not comparable. To investigate the robustness of this approach—and, in particular, to investigate whether competing causes of death would affect our results—we used Cox regression modeling to estimate hazard ratios (HRs) for comparison with ORs. 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. In models in which the HR for a covariate was not constant over time, we included an interaction term of the covariate and time in the model. The choice of regression model made little difference to our conclusions.

Clustering effects may have arisen because most participants in the cohort belonged to families that included other cohort
members, and, therefore, the cohort participants shared childhood conditions and possible genetic effects on cancer. We calculated robust SEs by using the “repeated” option for PROC GENMOD and the “id” option for PROC PHREG in SAS to allow for a between-family component of variation.

Because age is a strong determinant of mortality risk and because energy intake was associated with dairy intake and cancer mortality in this population (43), we controlled for age, sex, and energy intake (continuous) in a basic model. In an expanded multivariate model, we explored the confounding effect of the following factors measured in childhood: fruit, vegetable, and fat intakes; weight and height; district and season of the survey; SES (determined from the occupation of the head of the household); and per capita 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 the British Health Authority area of residence at the time of death, emigration, or participation in follow-up study in 1998 were used as a proxy for SES in adulthood (44). These covariates were retained in the model if they changed the OR estimate of the highest compared with the lowest intake group by >10%. Because dairy intake varied by survey district, all models were also evaluated with stratification for this variable.

We analyzed associations between total dairy intake and cancer risk among individuals with dairy intake and cancer risk to determine whether particular dairy products could explain the associations. We also repeated the multivariate model with additional inclusion of calcium and protein intake to investigate whether associations between dairy intake and cancer risk could be explained by the calcium or protein content of dairy foods. Associations between calcium intake and cancer risk were assessed after correction for confounders to determine whether calcium was associated with cancer risk independent of dairy intake. Associations between dairy intake and colorectal cancer were further adjusted for childhood meat intake, because high meat consumption is a known risk factor for that disease (45). Fat and calcium were included in the models as unadjusted nutrients, because the correlation between these nutrients and energy intake was corrected for by inclusion of energy in all multivariate models.

To assess whether associations between childhood dairy intake and adult cancer risk may be mediated by IGF-1 concentration, we used linear regression analysis to examine the association between childhood dairy intake and adult height, which is a marker for childhood IGF concentrations (46). To assess whether associations between childhood dairy intake and adult cancer risk were confounded by smoking status, we repeated the analyses in the subgroup of 1626 participants who provided information about their smoking behavior (current, past, or never) in a follow-up data collection in 1997.

A test for linear trend was obtained by modeling 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 Inc, Cary, NC). All reported P values are 2-sided.

## RESULTS

The baseline characteristics of the study population by total dairy intake group are shown in Table 1. The median daily intake of dairy products ranged from 89 g/d in the lowest group to 471
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<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>P for trend</th>
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<tr>
<td>All</td>
<td>198</td>
<td>215</td>
<td>178</td>
<td>179</td>
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<td>Basic OR‡</td>
<td>1.00</td>
<td>1.09 (0.86, 1.38)‡</td>
<td>0.87 (0.69, 1.10)</td>
<td>0.78 (0.60, 1.02)</td>
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<td>0.84 (0.64, 1.10)</td>
<td>0.09</td>
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<tr>
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<td>1.11 (0.87, 1.42)</td>
<td>0.94 (0.72, 1.21)</td>
<td>0.89 (0.61, 1.29)</td>
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<tr>
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<td>27</td>
<td>18</td>
<td>26</td>
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<tr>
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<td>1.03 (0.57, 1.87)</td>
<td>0.69 (0.37, 1.28)</td>
<td>0.93 (0.47, 1.82)</td>
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<td>1.02 (0.56, 1.86)</td>
<td>0.67 (0.35, 1.25)</td>
<td>0.89 (0.45, 1.75)</td>
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<td>1.13 (0.61, 2.09)</td>
<td>0.80 (0.41, 1.58)</td>
<td>1.35 (0.54, 3.39)</td>
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<td></td>
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<td>17</td>
<td>30</td>
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<tr>
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<td>1.45 (0.68, 3.07)</td>
<td>1.46 (0.70, 3.07)</td>
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<td>1.47 (0.69, 3.12)</td>
<td>1.59 (0.75, 3.35)</td>
<td>2.90 (1.26, 6.65)</td>
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<td>1.89 (0.82, 4.36)</td>
<td>4.31 (1.30, 14.22)</td>
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<td>0.56 (0.22, 1.45)</td>
<td>0.31</td>
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<tr>
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<td>0.83 (0.34, 1.99)</td>
<td>0.89 (0.38, 2.11)</td>
<td>0.55 (0.21, 1.42)</td>
<td>0.30</td>
</tr>
<tr>
<td>Multivariate plus calcium‡</td>
<td>1.00</td>
<td>0.75 (0.30, 1.84)</td>
<td>0.74 (0.29, 1.88)</td>
<td>0.34 (0.11, 1.04)</td>
<td>0.20</td>
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<td>Lung</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases (n)</td>
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<td>47</td>
<td>35</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Basic OR‡</td>
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<td>1.06 (0.68, 1.64)</td>
<td>0.77 (0.49, 1.22)</td>
<td>0.56 (0.33, 0.93)</td>
<td>0.01</td>
</tr>
<tr>
<td>Multivariate‡</td>
<td>1.00</td>
<td>1.09 (0.70, 1.69)</td>
<td>0.90 (0.57, 1.44)</td>
<td>0.66 (0.39, 1.10)</td>
<td>0.09</td>
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<tr>
<td>Multivariate plus calcium‡</td>
<td>1.00</td>
<td>0.98 (0.62, 1.53)</td>
<td>0.73 (0.45, 1.19)</td>
<td>0.38 (0.19, 0.75)</td>
<td>0.01</td>
</tr>
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<td>Stomach</td>
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<tr>
<td>Cases (n)</td>
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<td>9</td>
<td>10</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Basic OR‡</td>
<td>1.00</td>
<td>1.00 (0.35, 2.85)</td>
<td>1.08 (0.39, 3.10)</td>
<td>0.40 (0.10, 1.58)</td>
<td>0.23</td>
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<tr>
<td>Multivariate‡</td>
<td>1.00</td>
<td>1.01 (0.36, 2.85)</td>
<td>1.11 (0.40, 3.10)</td>
<td>0.42 (0.10, 1.71)</td>
<td>0.26</td>
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<tr>
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<td>1.00</td>
<td>1.17 (0.39, 3.47)</td>
<td>1.46 (0.44, 4.89)</td>
<td>0.81 (0.09, 7.34)</td>
<td>0.79</td>
</tr>
</tbody>
</table>

† Total median dairy intake was 89, 163, 255, and 471 g/d in group 1, 2, 3, and 4, respectively. All ORs were from logistic regression analysis.
‡ Adjusted for age, sex, and energy intake.
§ OR; 95% CI in parentheses (all such values).
¶ Adjusted for age, sex, and energy and fruit intakes.
\(^{5}\) Adjusted for age, sex, and energy, fruit, and calcium intakes.

g/d in the highest group. On average, 94% of dairy intake was due to milk consumption. Children in the highest dairy intake group were taller, more likely to be in a household with high food expenditure during childhood, and less likely to live in a deprived area as an adult than were those in the lowest intake group (P for trend <0.0001 for all). The former group also had higher intakes of fruit, eggs and egg dishes, calcium, and total energy (P for trend <0.0001); moreover, 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 <0.0001).

Group differences in age and in vegetable and fat intakes did not show clear patterns. Dairy intake was highly correlated with total calcium intake (Spearman correlation coefficient: 0.91).

In total, 273 incident cancers (registrations) and 497 deaths from cancer were identified in 4374 participants in the follow-up period. Most prominent among the cancers were breast cancer (53 registrations, 45 deaths), colorectal cancer (35 registrations, 41 deaths), prostate cancer (17 registrations, 24 deaths), lung cancer (9 registrations, 147 deaths), and stomach cancer (3 registrations, 29 deaths). One breast cancer death and 3 lung cancer deaths were secondary to earlier registration of a different cancer type, and these cases were excluded from the analyses.

**Total dairy intake**

The ORs for each cancer type and all cancers combined across levels of total dairy intake are shown in Table 2. Adjustment for fruit intake attenuated a weak inverse association between overall cancer risk and dairy consumption (multivariate OR for the highest versus the lowest intake group: 0.84; 95% CI: 0.64, 1.10; P for trend = 0.09); further adjustment for calcium intake abolished the association (P = 0.40). There was no evidence of confounding by weight; height; season of survey; vegetable, egg, or fat intake; or socioeconomic indicators in childhood or adulthood. Stratification by survey district did not alter the risk estimates. Dairy intake was not associated with breast or stomach cancer risk.

High dairy intake was associated with a near-tripling in the odds of colorectal cancer (multivariate OR: 2.90; 95% CI: 1.26, 6.65; P for trend = 0.005) compared with low dairy intake. There...
may have been negative confounding by calcium intake, because, after additional correction for this covariate, there was an even stronger association between dairy intake and colorectal cancer risk (multivariate- plus calcium-adjusted OR for highest versus lowest dairy group: 4.31; 95% CI: 1.30, 14.22; P for trend = 0.007). Calcium intake did not have a clear independent association with colorectal cancer risk in this population (multivariate-adjusted OR for highest versus lowest intake: 1.91; 95% CI: 0.84, 4.32; P for trend = 0.18). Analysis using Cox regression produced results similar to those obtained from logistic regression: the multivariate- plus calcium-adjusted HR for the highest versus lowest dairy group was 3.98 (95% CI: 1.50, 10.64; P for trend = 0.01). Further adjustment for protein and meat intakes, household food expenditure in childhood, or Townsend deprivation score (in adulthood) did not appreciably change these estimates.

The risk of prostate cancer was considerably lower in those with high dairy intakes, and it showed a dose-response effect. However, because of the small number of cases (n = 41), evidence against the null hypothesis of no association was weak (multivariate- plus calcium-adjusted OR for highest versus lowest dairy group: 0.34; 95% CI: 0.11, 1.04; P for trend = 0.20). Further adjustment for protein intake or Townsend deprivation score did not appreciably change this estimate, but the association was abolished after adjustment for household food expenditure in childhood (multivariate- plus calcium-adjusted OR for highest versus lowest dairy group: 0.41; 95% CI: 0.14, 1.26; P for trend = 0.32). Cox regression analysis showed similar results (not shown).

Lung cancer risk had a negative association with dairy intake after adjustment for calcium and other confounders; similar results were obtained by Cox regression analysis (multivariate-plus calcium-adjusted HR for highest versus lowest dairy group: 0.44; 95% CI: 0.21, 0.92; P for trend = 0.04). We investigated this association further in the subgroup of 1626 participants who provided information about their smoking behavior (current, past, or never) in a follow-up data collection in 1997. These analyses indicated that the association between childhood dairy intake and lung cancer was confounded by smoking status in adulthood. For example, the multivariate- and calcium-adjusted HR for the highest versus lowest dairy group (300 g/d) smokers. Smoking status did not confound the associations between childhood dairy intake and adult risk of breast, colorectal, prostate, or stomach cancer or all cancer types combined.

### Milk Intake

Associations between childhood milk intake and cancer risks were very similar to those shown above (Table 3). A modest inverse association with overall cancer risk was abolished after adjustment for calcium and protein intake. A positive dose-response relation with colorectal cancer risk remained after a similar adjustment (P for trend = 0.02), with OR estimates close to those for total dairy intake. Compared with participants in the lowest milk intake group (<0.5 cups/d), those in the highest milk intake group (≥1.2 cups/d) had a significantly lower risk of prostate cancer (multivariate- plus calcium-adjusted OR: 0.24; 95% CI: 0.08, 0.70), although there was no clear dose-response relation. This inverse association was not confounded by household food expenditure in childhood. Associations for lung cancer with milk intake were the same as those for dairy intake. Milk consumption was not associated with breast or stomach cancer. Further adjustment for protein intake did not appreciably change these estimates.

### Other Dairy Products and Dietary Factors

Participants who consumed the greatest amount of cream (>7 tablespoons/wk) had a multivariate- and calcium-adjusted OR of 3.46 (95% CI: 1.19, 10.06; P for trend = 0.005) for all cancers combined versus participants consuming <1.5 teaspoons cream/wk. High intake of cream was also associated with a greater risk of lung cancer, but CIs were very wide (data not shown). Cream intake showed no relation to breast and colorectal cancer; estimates for prostate and stomach cancer are unavailable because the small numbers in the study made the regression model unstable. There were no associations between childhood consumption of cheese, milk pudding, or ice cream and adult cancer risk (data not shown).

There were no independent associations between total calcium intake and the risk of any of the cancer types (data not shown), apart from weak evidence of an inverse association with prostate cancer risk (multivariate- plus dairy intake-adjusted OR for highest versus lowest group: 0.35; 95% CI: 0.08, 1.47; P for trend = 0.08).

Children in the highest dairy intake group also achieved taller heights in adulthood than did those in lower dairy intake groups; in a follow-up study of 1604 Boyd Orr study participants in 1997, mean self-reported age-adjusted heights were 165.4 cm in those who had been in the lowest and 166.7 cm in those who had been in the highest childhood dairy intake group (P for trend = 0.02). However, this association disappeared after adjustment for household food expenditure or SES in childhood.

### DISCUSSION

The results of our 65-y follow-up study of children born in the 1920s or 1930s suggest that a family diet rich in dairy foods during childhood is associated with a substantially increased risk of colorectal cancer risk in adulthood. The association was independent of childhood meat, fruit, and vegetable intakes; SES in childhood and adulthood; and other risk factors. This increased risk appears to be in sharp contrast with the steadily increasing pool of evidence of a protective effect of dairy consumption on colorectal cancer risk in adult populations (34–37). Our finding that high childhood intake of milk is associated with lower prostate cancer risk is also contrary to findings in adult intake studies (23, 33).

The association of a greater risk of colorectal cancer with high childhood dairy intake seen in this study was strengthened after further adjustment for calcium intake, which suggested that there was negative confounding by calcium intake. Calcium intake did not have a clear independent association with colorectal cancer risk in this population, but, because of the high correlation between calcium and dairy intake, it is difficult to fully determine the independent effects of these dietary exposures in our data. Our study did not show any associations between childhood dairy consumption and breast cancer risk, and thus it conflicts with the findings of Hjartaker et al (28). A recent meta-analysis
shown that adult IGF-I concentrations are associated with premenopausal but not with postmenopausal breast cancer (12). We were not able to distinguish premenopausal from postmenopausal cases of breast cancer in our study population, and age-specific analyses were not possible because of the small numbers. Thus, a dilution of subtle associations with premenopausal breast cancer may have occurred.

Possible mechanisms

Although the biological mechanisms that may underlie our findings cannot be determined from our study, we propose that the associations between dairy intake in childhood and the risk of colorectal and prostate cancer in adulthood may have to do with the programming effects of early-life nutrition on the IGF system or other pathways.

Our observation that a high intake of dairy foods in childhood is associated with a substantially greater risk of colorectal cancer in adulthood may indicate that it is the effect of childhood dairy intake on childhood (rather than on adult) concentrations of IGF-I that is the important mediator of future risk. This may have to do with the positive association between dairy intake and IGF-I concentrations in childhood (18), the inverse association between childhood dairy intake and adult IGF-I concentrations (20), and the positive link between adult IGF-I concentrations and colorectal cancer risk (11). An alternative biological mechanism may be early-life programming effects, possibly involving the vitamin D pathway. The process of colonic formation of 1,25(OH)₂D, which helps colon cells avoid hyperproliferation and prevents their progression into malignancy (48), is probably under epigenetic regulation (49). The early postnatal period is a period of physiologic plasticity, and diets in early childhood can affect disease risk in adulthood (50)—eg, through epigenetic imprinting of genes (51). There is some indirect evidence that epigenetic regulatory mechanisms in the gastrointestinal tract continue to develop in the postnatal period (52), although we are not aware of specific effects of dairy consumption on these processes.

Our finding that the highest milk intake in childhood is associated with a lower risk of prostate cancer risk is contrary to findings in adult intake studies (23, 33) but is in keeping with the possible long-term programming effect of childhood nutrition on adult IGF-I (19, 21, 22) and with the inverse association between childhood dairy intake and adult IGF-I concentrations observed in the population of the present study (20). Recent genetic analyses have confirmed a role for IGF-I in prostate cancer risk by showing that inherited variations in IGF-I may play a role in the risk of prostate cancer (53).

Study strengths and limitations

This study has several strengths. First, diet was measured in childhood long before the occurrence of disease, which averted the problem of recall bias that is encountered in studies based on
remembering childhood diet (28, 30, 54). Second, all foods consumed in the home were assessed, which allowed the consideration of other dietary factors—eg, fruit and vegetable intakes—as potential confounders of the relation between dairy intake and cancer risk. Third, our estimates of family milk consumption were reliable: in a study of 195 families who kept 2 inventories between 3 and 15 mo apart, repeatability was high for milk intake (intraclass correlation coefficient: 0.85) (55).

It is important, however, to interpret these results in light of the study limitations. First, childhood diet was based on household rather than individual consumption. Nevertheless, misclassification resulting from imprecise diet measurements would likely have been nonsystematic, attenuating rather than explaining the associations observed. Moreover, our previous finding in this population—that energy intake in childhood was positively associated with cancer risk (43)—was consistent with other evidence (56) and thus provided support for the reliability of our dietary estimates. We expect that, more so than other foods, dairy products were consumed by the children of the families in the Boyd Orr Study; thus, we have greater confidence in attributing dietary estimates. We expect that, more so than other foods, dairy intake (intraclass correlation coefficient: 0.85) (55).

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Because repeat assessments of diet during the life course are not available for most of the participants, we are unable to discern whether some of these associations are confounded by dietary habits in adulthood, which may have been correlated with childhood diet (57), but which 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), and thus these results probably cannot be explained by similar dairy consumption patterns in adulthood, and they likely point to a childhood-specific effect. The long-term and probably subtle effects of childhood diet on adult cancer risk may have been negated by the perhaps much stronger effects of the longer-term adult dietary habits.

The strongest associations with cancer risk in this study are seen with total dairy and milk intakes in the highest intake groups. The 2 highest groups of milk intake equated to a median milk intake of 1 cup/d and 1.9 cups/d, respectively. These milk consumption levels are similar to current estimates for US children [average consumption: ≈1.6 servings milk/d (58)]. Thus, the associations in our data occur at intakes that are similar to current "normal " intakes.

Conclusions

In conclusion, we found some evidence of a greater risk of colorectal cancer and weak evidence of a lower risk of prostate cancer associated with a family diet rich in dairy foods during childhood. There was no evidence for an independent association between adult cancer risk and a family diet rich in calcium during childhood. These results are in the opposite direction of associations between adult dairy consumption and the risks of colorectal and prostate cancer. The possibility that early-life programming effects are underlying these associations cannot be confirmed from our study, but that hypothesis warrants further investigation. 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. More evidence from studies including a more complete life-course assessment of dairy intake and related dietary and lifestyle factors is needed before any firm conclusions can be drawn.

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The authors’ responsibilities were as follows—JCvdP: the data analysis and writing of the manuscript; CB: preparation of the food diaries for data analysis and contributions to the analysis plan and writing of the manuscript; DG and RMM: study design, analysis plan, and writing of the paper; GDS: establishment of the Boyd Orr cohort and writing of the manuscript; and CF: preparation of the food diaries data for analysis and contributions to writing of the manuscript. None of the authors had any personal or financial conflict of interest.

REFERENCES


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