# POSITION STATEMENT
## Dairy foods, calcium and cancer prevention

### Key messages

- Calcium is an important nutrient for bone and dental health, with dairy foods being the major source of dietary calcium in Australia. Dairy foods such as milk, yoghurt and cheese are also good sources of calcium, protein, vitamin A, vitamin B12, magnesium, phosphorus, potassium, riboflavin and zinc.
- In terms of cancer risk, dairy foods and calcium have shown both protective and harmful effects. Overall the proven health benefits of dairy foods outweigh the unproven harms.
- The evidence suggests that milk *probably* protects against colorectal cancer, and there is *limited suggestive* evidence that milk reduces the risk of bladder cancer.
- There is *limited suggestive* evidence that milk and dairy foods increase the risk of prostate cancer, and cheese increases the risk of colorectal cancer.
- There appears to be no significant association between the consumption of dairy products and the risk of breast or ovarian cancer.
- Calcium supplements *probably* protect against colorectal cancer. However diets high in calcium have been linked with a *probable* increase in the risk of prostate cancer. Therefore there is still insufficient evidence to recommend the general use of calcium supplements for cancer prevention.
- Dairy foods should be encouraged as part of a varied and nutritious diet as they are essential to maintain good bone and dental health.
- Cancer Council supports the Australian Dietary Guidelines, which encourage people to eat at least three serves of dairy foods (milk, cheese and yoghurt) each day.
- Cancer Council encourages people to choose reduced fat varieties of dairy foods where appropriate.

### Rationale

Dairy foods provide the richest source of dietary calcium.[1] Dairy foods contain a high calcium content per serve and this calcium is well absorbed by the body.[1] Calcium from non-dairy sources is less concentrated, and therefore more of the food needs to be consumed to meet recommended levels.[2,3] Dairy foods also provide significant amounts of other nutrients including protein, vitamin A, vitamin $B_{12}$, magnesium, phosphorus, potassium, riboflavin and zinc. In addition, dairy products contain conjugated linoleic acid, butyric acid, sphingolipids and 13-methyl tetradecanoic acid which may have anti-cancer properties.[4]

The role of dairy foods in bone health is well established. In addition to playing an important role in the prevention of osteoporosis, dairy foods are essential for good dental health. There is also some evidence that dairy foods may play a role in weight regulation,[5] prevention of cardiovascular disease and in management of hypertension.[6]

Unfortunately, there is a lot of misinformation regarding the relationship between dairy foods and cancer risk. It is important for Cancer Council to evaluate the association between dairy foods, calcium and cancer risk in order to develop clear messages and recommendations. Evidence for the role of dairy foods in cancer mostly relates to prostate, colorectal and breast cancers, the most prevalent cancers in Australia, as well as ovarian cancer.

## Background

Dairy foods include foods such as milk, yoghurt, cheese, ice cream, butter, cream and fermented milk. Table 1 shows the calcium content of some common dairy foods.

**Table 1.** Average calcium content of dairy foods[7]

| Food Source | Serve Size | Calcium |
|---|---|---|
| Regular milk | 250 mL | 285 mg |
| Skim milk | 250 mL | 308 mg |
| Natural regular yoghurt | 200 g | 342 mg |
| Natural low fat yoghurt | 200 g | 418 mg |
| Cheddar cheese | 40 g | 310 mg |
| Ice cream (standard vanilla) | 50 g | 60 mg |

In addition to dairy foods, calcium fortified products are increasing in the food supply and include: 1 cup (40 g) calcium fortified breakfast cereals (contains up to 200 mg of calcium); ½ cup (100mL) calcium fortified orange juice (80 mg calcium); 2 slices (30 g) calcium fortified bread (200 mg calcium); 250 mL calcium fortified soy milk (296 mg calcium).

According to the last National Nutrition Survey in 1995, dairy products were the second greatest contributor to energy intake for both men and women, accounting for about 11% of total energy intake.[8] Dairy products also accounted for more than half the daily calcium intake, with 30-45% coming from milk, about 10% from cheese and about 5% from frozen milk products.[8] The contribution of dairy products to children's calcium intake was much greater than for adults.[8]

Three to four serves of dairy foods per day provide the recommended daily calcium intake for adults.[9] The current Recommended Dietary Intake (RDI) for men is 1000 mg/day for those aged 19-70 years and 1300 mg for those aged over 70 years.[10] For women, the RDI is 1000 mg/day for those aged 19-50 years and 1300 mg for those aged over 50 years (post menopausal).[10] The new nutrient reference values for Australians no longer recommend increased calcium requirements for pregnant and lactating women over the age of 18.[10]

The upper dietary intake limit for calcium for adults has been proposed at 2500 mg/day.[10] Toxic effects of calcium have only been seen when calcium is given as calcium carbonate in an antacid form. The resulting hypercalcaemia can cause renal calcification and renal failure.[10]

In Australia, dietary calcium intakes are less than recommended. It is estimated that more than 25% of men and 50% of women have a calcium intake below the RDI.[8] Of concern are those not receiving sufficient calcium during the years of bone modeling and those older Australians who are at risk of osteoporosis. Dairy foods provide a number of other important nutrients including protein, phosphorus, magnesium, potassium and zinc which are needed for bone development and maintenance. Vitamin D, which is found in small amounts in fortified dairy products (for Australians the main source of Vitamin D is from exposure to sunlight) plays an important role in maintaining bone health.[11, 12]

## Views on dairy and calcium in the major cancer prevention reports

In 2007, the World Cancer Research Fund found there was:[13]

- *Probable* evidence that milk reduced the risk of colorectal cancer, and *limited suggestive* evidence that milk lowered the risk of bladder cancer
- *Limited suggestive* evidence that milk and dairy foods increased the risk of prostate cancer and that cheese increased the risk of colorectal cancer
- *Probable* evidence that diets high in calcium increased the risk of prostate cancer and that calcium supplements lowered the risk of colorectal cancer.

The World Health Organization concluded in 2003 that there is some evidence that the risk of colorectal cancer is decreased by high intakes of calcium.[14] This hypothesis however, has not been firmly established. Several observational studies have provided support for this theory, and two trials have indicated that supplemental calcium may have a modest protective effect on the recurrence of colorectal adenomas.

## Epidemiological evidence

### Colorectal cancer

A systematic review of 12 cohort studies found that nine studies did not show a significant relationship between milk consumption and risk of colorectal cancer and two reported a protective effect for colorectal and colon cancer.[15] One study with a relatively small cohort size (<10,000 participants) found a positive relationship between dairy foods and rectal cancer. One study found a borderline positive relationship in women between cheese intake and rectal cancer, while five studies showed no relationship between dairy products and colorectal cancer. Therefore consumption of dairy products appears unrelated to colon cancer, although a harmful effect on rectal cancer risk cannot be excluded.[15]

A pooled analysis of ten cohort studies found that higher intakes of milk and calcium (from diet and supplements) were associated with a reduced risk of colorectal cancer.[16] While cheese intake tended to be weakly positively associated with colorectal cancer risk, yoghurt had a weak inverse association, with neither result being statistically significant.[16] Higher intakes of dietary and total calcium were associated with a significant lower risk of colorectal cancer (table 2).[16] This study estimated that up to 1000 mg/day of calcium is required to protect against colorectal cancer.[16]

A recent meta-analysis of three randomised controlled trials (RCTs) investigating the role of calcium supplementation in preventing colon adenoma recurrence showed a significantly decreased risk of recurrent adenoma in the group receiving calcium supplementation (table 2).[17] In addition, a Cochrane review, which included two double-blind, placebo-controlled RCTs suggested that calcium supplementation can provide some protection against the recurrence of colorectal polyps (table 2).[18] Although the results look promising for calcium supplementation, further research is required before it is recommended to prevent colorectal cancer.

**Table 2.** Summary relative risk (RR) and odds ratio (OR), 95% confidence interval (CI) and *p* values for dairy food consumption and colorectal cancer risk[16-18].

| Study | Outcome | Food | RR/OR | 95% CI | p | Conclusion |
|---|---|---|---|---|---|---|
| Cho et al. (2004)[16] | Colorectal cancer | Dietary calcium | 0.86 | 0.78-0.95 | <0.02 | Statistically significant negative association |
| | | Total calcium (dietary and supplemental) | 0.78 | 0.69-0.88 | <0.001 | |
| Shaukat et al. (2005)[17] | Colon adenoma recurrence | Calcium supplement | 0.80 | 0.68-0.93 | <0.001 | Statistically significant negative association |
| Weingarten et al. (2005)[18] | Colorectal polyp recurrence | Calcium supplement | 0.74 | 0.58-0.95 | - | Negative association |

## Breast cancer

A 2005 review on the consumption of dairy foods and risk of breast cancer identified 39 case-control and 11 cohort studies.[19] Both case-control and cohort studies provided inconsistent evidence, leading the authors to conclude that there was no evidence to support an association between consumption of dairy products and breast cancer risk.[19]

An earlier review commissioned by the Dairy Council of Britain identified 36 case-control and ten cohort studies.[20] A statistically significant inverse relation between breast cancer and dairy product consumption was reported in each of the cohort studies. Case-control studies revealed inconsistent evidence. Overall there was no association found between the consumption of milk or other dairy products and the risk of breast cancer.[20]

A meta-analysis published in 1993 included ten case-control and one cohort study on the association between cheese and milk intake with breast cancer risk.[21] The relative risks suggest that higher intakes of milk and cheese are associated with a non-significant increased risk of breast cancer (table 3).[21]

Ten years later another meta-analysis, which included 14 case-control and five cohort studies, updated and expanded on the earlier report.[22] The evidence from case-control studies and cohort studies was found to be inconsistent regarding milk consumption and breast cancer risk. Case-control studies suggested an increased risk of breast cancer, but the cohort studies showed a protective association. The pooled results for both case-control and cohort studies showed an increased risk of breast cancer with cheese consumption.[22] Once again, the results suggest that a higher intake of total milk and cheese is associated with a non-significant increased risk of breast cancer (table 3).[22]

A meta-analysis of data from eight prospective cohort studies did not find an association between dairy products, analysed as total dairy fluids and total dairy solids, and the risk of breast cancer.[23] There was however, an increased risk of breast cancer with cheese consumption, although this was not statistically significant (table 3).[23]

**Table 3.** Summary relative risk (RR), 95% confidence interval (CI) and *p* values for dairy food consumption and breast cancer risk.[21-23]

| Study | Food | RR | 95% CI | p | Conclusion |
|---|---|---|---|---|---|
| Boyd et al. (1993)[21] | Milk | 1.22 | 0.91-1.64 | - | No statistically significant association |
| | Cheese | 1.32 | 0.90-1.93 | - | |
| Boyd et al. (2003)[22] | Milk | 1.12 | 0.88-1.43 | - | No statistically significant association |
| | Cheese | 1.30 | 0.89-1.92 | - | |
| Missmer et al. (2002)[23] | Total dairy fluids | 0.99 | 0.97-1.00 | 0.25 | No statistically significant association |
| | Total dairy solids | 1.03 | 0.95-1.11 | 0.43 | |
| | Milk products | 0.99 | 0.97-1.00 | 0.24 | |
| | Cheese | 1.16 | 0.98-1.37 | 0.50 | |

## Ovarian cancer

A pooled analysis of 12 cohort studies found no statistically significant associations between the consumption of dairy foods, specifically milk, cheese, yoghurt and ice cream, dietary calcium intake and total calcium intake and the risk of ovarian cancer (table 4).[24]

Another meta-analysis examined three cohort and 18 case-control studies alone and in combination.[25] The cohort studies tended to show that high intakes of dairy foods (at least four servings) may increase the risk of ovarian cancer, however these results were not significant.[25] In a combined analysis of case controls and cohort studies, the consumption of dairy products, whole milk and yoghurt were positively but not significantly associated with a modest increased risk of ovarian cancer.[25] The consumption of milk, skim milk, and cheese were inversely associated with ovarian cancer risk (table 4).[25]

A later meta-analysis pooled data from two cohort and 20 case-control studies, to evaluate the risk of ovarian cancer associated with milk and dairy product consumption.[26] It should be noted that some of the summary relative risks for particular dairy items were combined from only a few studies (5-8 studies), which may limit the validity. This meta-analysis found that the consumption of dairy products, whole milk and butter were associated, but not significantly, with increased risk of ovarian cancer (table 4).[26] However, overall there was no association between milk and dairy product consumption and the risk of ovarian cancer.[26]

**Table 4.** Summary relative risk (RR), 95% confidence interval (CI) and *p* values for dairy product intake and risk of ovarian cancer.[24-26]

| Study | Food | RR | 95% CI | Conclusion |
|---|---|---|---|---|
| Genkinger et al. (2006)[24] | Total milk | 1.11 | 0.87-1.41 | No statistically significant association |
| | Hard cheese | 1.30 | 0.96-1.78 | |
| | Yoghurt | 1.04 | 0.86-1.24 | |
| | Dietary calcium | 1.17 | 0.93-1.47 | |
| | Total calcium | 1.08 | 0.84-1.38 | |
| Larsson et al. (2006)[25] | Dairy products | 1.17 | 0.85-1.60 | No statistically significant association |
| | Milk | 0.87 | 0.68-1.10 | |
| | Whole Milk | 1.25 | 1.01-1.56 | |
| | Skim/low fat milk | 0.94 | 0.75-1.17 | |
| | Yoghurt | 1.13 | 0.96-1.33 | |
| | Cheese | 0.95 | 0.80-1.12 | |
| Qin et al. (2005) [26] | Dairy products | 1.25 | 0.76-2.08 | No statistically significant association |
| | Milk | 0.81 | 0.61-1.07 | |
| | Whole milk | 1.22 | 0.94-1.59 | |
| | Skim milk | 0.89 | 0.65-1.21 | |
| | Yoghurt | 1.11 | 0.97-1.26 | |
| | Cheese | 0.93 | 0.75-1.17 | |
| | Butter | 1.24 | 0.89-1.70 | |

## Prostate cancer

A meta-analysis evaluated the association between milk consumption and prostate cancer exclusively from case-control studies.[27] A positive association between milk and dairy consumption and prostate cancer risk was found, however many of the studies were found to be subject to bias (table 5).[27] In addition, eight of these studies used hospital-based controls, which may not be representative of the general population.

A second meta-analysis of ten cohort studies found that men with the highest intake of dairy foods and calcium were significantly more likely to develop prostate cancer than men with the lowest intake (table 5).[28] However this result was not significant when only those studies with a validated food frequency questionnaire and those that adjusted for energy intakes were considered.

This meta-analysis was recently reviewed in response to criticism that it did not include data from the Melbourne Collaborative Cohort Study (MCCS). The MCCS is a large prospective study, which did not find any association between dairy products, butter, margarine and calcium intakes and the risk of prostate cancer.[29]

When the results of the MCCS were included in the meta-analysis, the positive association between a high dairy intake and prostate cancer risk remained, however it was no longer statistically significant.[30] This positive association was also attenuated for high calcium intakes (table 5).[30]

**Table 5.** Summary relative risk (RR) and odds ratio (OR), 95% confidence interval (CI) and *p* values for dairy food consumption and prostate cancer risk.[27, 28, 30]

| Study | Food | RR/OR | 95% CI | p | Conclusion |
|---|---|---|---|---|---|
| Qin et al. (2004)[27] | Milk | 1.68 | 1.34-2.12 | - | Positive association |
| | Milk and dairy products | 1.61 | 1.22-2.12 | - | |
| Gao et al. (2005)[28] | Dairy products | 1.11 | 1.00-1.22 | 0.047 | Statistically significant positive association |
| | Calcium | 1.39 | 1.09-1.77 | 0.018 | |
| Gao et al. (2006)[30] | Dairy products | 1.09 | 1.00-1.20 | 0.059 | Positive association |
| | Calcium | 1.32 | 1.05-1.67 | 0.026 | Statistically significant positive association |

An RCT suggests there is no increase in prostate cancer risk associated with calcium supplementation.[31] The 672 men were randomly assigned to receive either three grams of calcium carbonate (1200mg calcium) or placebo daily for four years. After a mean follow-up of ten years, there were 33 prostate cancer cases in the calcium treated group and 37 in the placebo treated group (unadjusted rate ratio= 0.83, 95% CI= 0.52-1.32).[31]

Therefore, the risk of prostate cancer was moderately lower in the calcium-treated group, although this was not significant.[31] There was a statistically significant reduction in prostate cancer risk between baseline and year six (rate ratio= 0.52, 95% CI= 0.28-0.98) and between years two and six (rate ratio= 0.44, 95% CI= 0.21-0.94) in the calcium supplemented group.[31] However, these findings warrant further investigation before recommendations can be made regarding calcium supplementation and prostate cancer risk.

## Summary of the evidence from epidemiological studies

The evidence indicates that dairy products and an increased intake of calcium can reduce the risk of recurrent adenomas, the precursors of bowel cancer. There is still insufficient evidence however, to recommend calcium supplementation for cancer prevention.

There appears to be no significant association between the consumption of dairy products and the risk of breast and ovarian cancer.

There is some evidence to suggest that dairy and dietary calcium may be associated with an increased risk of prostate cancer.

## Potential mechanisms of action for cancer prevention

### Breast cancer

Experimental studies suggest that the presence of calcium, conjugated linoleic acid, butyric acid, branched long-chain fatty acids and milk proteins in dairy products have the potential to prevent breast cancer.

Calcium may neutralise fatty acids and mutagenic bile acids which pass from the intestine to the breast where they can affect estrogen receptors.[32] Animal studies provide evidence for anti-carcinogenic properties of calcium in the presence of vitamin D. Animals fed diets deficient in calcium and vitamin D develop mammary hyperplasia and hyperproliferation. In addition, supplementation with calcium and vitamin D protects against mammary tumours in rats fed a high fat diet or treated with a chemical carcinogen.[20]

Conjugated linoleic acid refers to a mixture of positional and geometric isomers of linoleic acid which are found in dairy products and meat. Animal studies have indicated that conjugated linoleic acid may inhibit the growth and spread of mammary tumours, possibly in a dose response relationship.[5] Epidemiology studies to date have provided inconsistent evidence. One study found no association between conjugated linoleic acid intake and the risk of breast cancer,[33] another showed a weak positive association,[34] and a third showed a 60% reduction in risk associated with higher intakes of conjugated linoleic acid.[35]

Butyric acid and milk proteins may also have anti-carcinogenic properties. Butyric acid, present uniquely in milk fat, induces differentiation and apoptosis, and inhibits proliferation in experimental studies.[32]

Branched-chain fatty acids are synthesized by rumen bacteria and are found in milk fat. 13-methyl-tetradecanoic acid has been found to induce cell death in human breast cancer cells by rapid induction of apoptosis.[32]

### Colorectal cancer

According to the results of experimental studies, the presence of sphingolipids, calcium, conjugated linoleic acid, butyric acid and lactic acid bacteria in dairy products have the potential to reduce colorectal cancer.

Sphingolipids are found in regular and reduced-fat dairy products. Evidence from animal studies suggests that sphingolipids suppress early markers of colon carcinogenesis and the appearance of advanced malignant tumours.[5]

It has been proposed that ionised calcium or calcium phosphate may reduce colon cancer by binding secondary bile acids and free fatty acids to form insoluble soaps.[36, 37] These insoluble soaps therefore protect the epithelial cells of the colon from potential toxic affects of the bile and free fatty acids.[38]

Butyric acid and conjugated linoleic acid may also play a role in protecting against colon cancer.[5]

There are several mechanisms by which lactic acid bacteria may inhibit colon cancer. Such mechanisms include the binding/degrading of potential carcinogens; changes in the metabolic activities of the intestinal microflora; and the production of anti-mutagenic compounds or enhancement of the host's immune response.[39]

### Ovarian cancer

It is thought that the vitamins found in milk have the potential to protect against ovarian cancer due to their antioxidant or anti-carcinogenic properties.[26] Calcium may play a protective role by down-regulating the production of parathyroid hormone, which reduces mitosis and increases apoptosis.[24]

## Potential mechanisms of action for cancer causation

### Dietary fat

Previously it was believed that dietary fat played a role in the development of breast cancer, due to the strong correlation between per capita consumption of fat and breast cancer mortality in ecological studies, and because animal experiments showed that a high fat diet increased the incidence of chemically induced tumors. However with increased epidemiological data, there now appears to be little association between cancer in adults and total fat or type of fat.[32] It is biologically plausible that fat may increase breast cancer risk from animal data. Potential mechanisms are thought to be through the development of free radicals, eicosanoids and mutagenic compounds from lipid peroxidation.[22]

### Contaminants

The incidence of breast cancer has declined in Israel since three pesticides, previously found in high concentrations in milk, were banned in the 1980s.[20] This decline in breast cancer incidence provided evidence for the role of dairy food contaminants in the risk of breast cancer. Evidence since this time suggests that there is no association between organochlorine exposure and breast cancer.[40] The 20th Australian Total Diet study 2003, formally the market basket survey, found no detection of pesticide residue in samples tested of cheddar cheese, whole milk and vanilla ice cream.[41] The study concluded that dietary exposures to pesticide residues in Australia were all within acceptable health standards.[41]

### Insulin Like Growth Factor-I and Growth Hormone

Insulin Like Growth Factor-I (IGF-I) has been suggested as a link between dairy product consumption and breast cancer risk.[42] However the amount of IGF-I consumed daily from milk products is minute compared with endogenous production.[32] There is little evidence to suggest that there is significant absorption from dairy foods, as it is broken down in the gut.[20] It appears that the evidence linking IGF-I in milk and breast cancer risk is weak.

Bovine somatotrophin or growth hormone has been implicated in the development of breast cancer.[42] In some countries growth hormone is administered to cows to increase milk production and it also increases milk IGF-I levels. However bovine somatotrophin has not been registered for use by the Australian Pesticides and Veterinary Medicines Authority (APVMA) for use in Australia. It is approved in the US and 24 other countries, but not approved for use in Australia, New Zealand, Canada or Europe.

### Lactose and galactose

The earliest link between dairy consumption and increased ovarian cancer was attributed to the lactose content of dairy.[43, 44] Lactose is converted to glucose and galactose. It was suggested that galactose consumption coupled with a reduced ability to metabolise galactose in the ovary would result in ovarian toxicity.[44] In addition to lactose, a high consumption of fat may also increase ovarian cancer risk through increased oestrogen levels, but this is inconclusive.[26]

## Recommendations

In terms of cancer risk, dairy foods and calcium have been reported as both protective and harmful. The evidence is not conclusive that dairy foods can protect against cancer, nor that they increase the risk. Overall the proven health benefits of dairy foods outweigh the unproven harms.

Dairy foods should be encouraged as part of a varied and nutritious diet as they are essential to maintain good bone and dental health. Cancer Council therefore supports the Australian Dietary Guidelines that encourage at least three serves of dairy foods (milk, cheese, yoghurt) each day.

Cancer Council also encourages people to choose reduced fat varieties of dairy foods where appropriate, as this will help to maintain a healthy body weight and reduce the total and saturated fat content of the diet. In addition, Cancer Council recommends that dairy foods such as cream and butter should be limited, as they contain a large amount of saturated fat.

Cancer Council does not support the use of calcium supplements for cancer prevention, but acknowledges that calcium supplementation provides an alternative source for people unable to consume enough dietary calcium (e.g. those who are lactose intolerant or who follow a strict vegan diet).

## Future research

The relationship between dairy foods and cancer, particularly breast, prostate and ovarian cancer deserves further examination due to the inconsistencies that still exist in the literature. As with many other nutritional factors, there is a need for better quality, well-reported, larger studies that are of longer duration. Studies need to be performed in populations with sufficient variation in dairy food intake.

A better understanding is required of the calcium dose that would be both safe and effective in reducing cancer risk, particularly for prostate and colorectal cancer. This requires appropriately designed randomised controlled trials before new public health recommendations regarding the optimal dose and duration of calcium supplementation can be made.

In addition, the protective constituents of dairy foods need to be identified to better understand the protective role of dairy foods, and the literature regarding probiotics and their role in cancer prevention, particularly colon cancer needs to be evaluated.


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