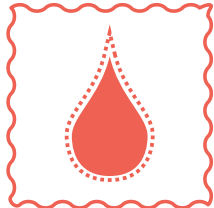




Dairy: good or bad for cancer prevention?



KEY MESSAGE

Total dairy intake, as well as intake of milk and dietary calcium, probably decreases the risk of developing colorectal cancer, while there is inconclusive evidence to support an association between dairy intake and the risk of breast or prostate cancer.

What is cancer?

The term 'cancer' refers to a group of more than 100 different diseases. Nonetheless, a relatively small number of functional abnormalities are typical of almost all solid tumours. These phenotypic characteristics of uncontrolled cell proliferation are called the eight 'hallmarks of cancer'. They include:

- evading growth suppressors
- avoiding immune destruction
- enabling replicative immortality
- activating invasion and metastasis
- inducing angiogenesis
- deregulating cellular energetics
- resisting cell death (apoptosis)
- sustaining proliferative signalling.

Together with two 'enabling characteristics', namely tumour promoting inflammation and genome instability and mutation, these factors are the core of cancer pathophysiology. The process starts with tumour initiation, proceeds with aspects such as tumour formation and progression, and ends with metastasis.

Although it is tempting to use the umbrella term 'cancer', it is more appropriate to specify a particular cancer, as the aetiology of the different types of cancer, including the link to diet, is specific to an organ site. Some cancers are associated with subtypes at a particular site, which may, in turn, have different nutrition-related causes.

How is diet linked to cancer?

It has been known for many years that about a third of the most common cancers can be prevented through diet, weight management and physical activity. As these are modifiable factors, lifestyle changes may ease the immense burden of cancer on individuals, families and healthcare systems. For this reason, the World Cancer Research Fund (WCRF), together with numerous international cancer institutes, has

compiled a decade-long effort of objective reviews and an expanding body of studies regarding the link between cancer and lifestyle factors such as diet, nutrition and physical activity into the so-called Third Expert Report, which was published in 2018. This report is universally acknowledged as the most authoritative and comprehensive reference in this field. (WCRF/American Institute for Cancer Research, 2018).

The aim of the current review is to summarise the findings that specifically relate to the association between intake of dairy and cancer from the global cancer report and 17 organ-specific continuous update projects (CUPs). Additional information from systematic reviews published from 2018 onwards is also incorporated.

Dietary patterns or foods can either increase or decrease the risk of developing cancer. Despite many studies being conducted each year to unravel the complex link between diet – including dairy consumption - and cancer, several questions remain unanswered. Confounding (i.e. when a third factor such as socioeconomic status, affects both the cancer and nutrition), effect modification (e.g. when the effect of nutrition differs for cancer in different stages of life, such as risk factors for pre- vs postmenopausal breast cancer) and research design considerations are major challenges. In the case of the link between diet and cancer, 'any evidence' is not good enough any more: the strength of evidence needs to be considered. In this review, only strong evidence (i.e. associations which are graded by the international WCRF panel as either convincing or probable) is reported.

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Scientists increasingly aim to explain the link between diet and cancer with reference to the 'hallmarks of cancer' mentioned earlier. Another trend is to move away from describing the link between nutrition and cancer in context of a bioactive compound or a nutrient-level approach. It seems unlikely that a particular food constituent is a true causal factor of cancer; rather, the food constituent (e.g. nutrient) is seen as a marker for the specific foods in which it is found. Thus, a *food-based approach*, and increasingly a *dietary pattern approach*, are favoured in describing the link between diet and cancer. In the case of dairy, studies increasingly differentiate between the products in this food group. For example, an investigation by Zhang et al. (2019) suggests specifically that intake of fermented dairy is associated with an overall decreased cancer risk.

Table 1

Dose–response meta-analyses linking dairy intake to cancer

Cancer type	Dairy 'exposure'	Intake per day	Risk estimate (95% CI)	Interpretation
COLORECTUM	Total dairy	400 g	0.87 (0.83–0.90)	A statistically significant 13% decreased risk of colorectal cancer per 400 g/d increase in total dairy intake
	Milk	200 g	0.94 (0.92–0.96)	A statistically significant 6% decreased risk of colorectal cancer per 200 g/d intake of milk
	Cheese	50 g	0.94 (0.87–1.02)	A non-significant association between risk of colorectal cancer per 50 g increase in cheese intake
	Dietary calcium	200 mg	0.94 (0.93–0.96)	A statistically significant 6% decreased risk of colorectal cancer per 200 mg increase in dietary calcium
BREAST (premenopausal)	Total dairy	200 g	0.95 (0.92–0.99)	Limited evidence to suggest a decreased risk
	Dietary calcium	300 mg	0.87 (0.76–0.99)	
BREAST (postmenopausal)	Dietary calcium	300 mg	0.96 (0.94–0.99)	Limited evidence to suggest a decreased risk
PROSTATE	Total dairy	400 g	1.07 (1.02–1.12)	Limited evidence to suggest an increased risk
	Dietary calcium	400 mg	1.05 (1.02–1.09)	

Source: Extracted from WCRF CUP report 'Meat, fish and dairy products and the risk of cancer', 2018

The current knowledge regarding the link between dairy intake and the risk of cancer is summarised quantitatively in Table 1 to translate the statistical estimate of risk into practical terms. The only strong evidence for a relationship between dairy intake and cancer is that total dairy, as well as the intake of milk and dietary calcium, **probably decreases the risk of developing colorectal cancer** (1:47).

The inverse relationship between dairy intake and colorectal cancer is largely associated with the calcium content of dairy and the presence of casein and lactose, which increases calcium bioavailability. In addition, lactic acid-producing bacteria in fermented dairy products, other nutrients and bioactive constituents in dairy may impart protection against colorectal cancer.

In a recent meta-analysis and systematic review, Barrubés et al. (2019) purposefully investigated the association between the intake of different dairy products and colorectal cancer location. Their findings consistently confirmed the information presented in Table 1, namely that high intakes of total dairy products and total milk are associated with a lower risk of colorectal cancer at any anatomic location. Consumption of low-fat milk was found to be associated with a reduced risk specifically for colon cancer, and cheese intake lowered the risk for proximal colon cancer. The latter was also reported by Zhang et al. (2019) in a random-effect meta-analysis that focused on the intake of various fermented dairy foods and they also highlighted a lowered risk for oesophageal and bladder cancer. Bermejo et al. (2019) cautiously came to a similar conclusion regarding bladder cancer, specifying that 'medium consumption of total dairy products and medium and high consumption of milk and fermented dairy products were associated with a decreased risk of bladder cancer'. As most studies to date have been conducted in developed

(industrialised) countries, El kinany et al. (2018) performed a systematic review of research regarding the association between the intake of dairy, whether modern or traditional products, and colorectal cancer in Middle Eastern and North African countries. The researchers concluded that results are currently inconsistent.

Findings of a recently published study by Sargsyan and Dubasi (2020) concur with those of the WCRF as presented in Table 1, namely that there is currently inconclusive evidence for an association between prostate cancer and dairy intake, although the fat content of the dairy product and the stage of prostate cancer were identified as potential modifying factors. In an overview of systematic reviews, Lopez-Plaza et al. (2019) included dairy product exposure (high compared with low intake), dairy product type (total dairy products, milk, cheese, yoghurt, and others) and prostate cancer outcomes (total, non-advanced, advanced prostate cancer and mortality) in their analysis of the relationship between prostate cancer and dairy intake. All relative risks of high compared with low intake (dose–response) for total prostate cancer ranged from 1.68 to 1.09 (1.07 per 400 g/day) for total dairy products, 1.50 to 0.92 (1.06 to 0.98 per 200 g/day) for milk (whole, low-fat and skim milk considered separately), and 1.18 to 0.74 (1.10 per 50 g/day) for cheese. Nonetheless, they concluded that the overall evidence is inconclusive. With regard to the limited evidence that suggests an increased risk of prostate cancer with higher dairy intakes, the WCRF proposes that the two potentially relevant hallmarks (1:30) involved in disease presentation are reduced apoptosis and increased proliferation due to higher IGF-1 levels and altered cell functioning. In a study focusing on testicular cancer, Signal et al. (2018) also concluded that their systematic review did not yield consistent evidence to link the intake of

milk, cheese, cream, butter or yoghurt to presentation of this cancer, either in a dose–response manner or over the course of life.

For most cancers, either no studies currently link dairy intake to cancer (largely because there is no reason to investigate such a relationship) or the existing studies point to an absence of an association. In a study not included in the WCRF report, Sergentanis et al. (2019) concluded from their systematic review that neither milk nor dairy product intake was associated with risk of non-Hodgkin lymphoma or leukaemia. Other cancer sites in this category include the stomach, liver, gallbladder, pancreas, kidney, ovary and endometrium.

Based on the findings as described here, **none** of the overall recommendations subsequently included in the 2018 WCRF report refer specifically to dairy.

Where does this leave us?

Diet and nutrition are only part of a suite of factors involved in the development of cancer. Other diseases, smoking tobacco, infections, family history of cancer, occupational exposures, radiation and medication may also be contributing factors, which can confound the link or modify the effect. Different components of the diet can affect cancers to a varying extent, and the same food or food group may increase the risk for one cancer yet simultaneously decrease the risk for another type of cancer. Different cancers, and even different subtypes of a cancer of the same organ, have different pathogeneses (for example, as seen in pre- and postmenopausal breast cancer). Numerous components of the diet may affect that same cancer. Diet and nutrition influence body weight, one of the most important factors in the development of cancer. A useful interactive tool developed by the WCRF (wcrf.org/matrix) shows the complex interactions between the dietary components related to cancer visually and Table 1 highlights the essence of current knowledge, showing the estimated risk in terms of the magnitude and direction of the link between dairy and dietary calcium intake and various cancers. We need to be wary of oversimplification and realise that much still needs to be uncovered through research.

In the meantime, the universal WCRF recommendations for cancer prevention through food, nutrition and physical activity should be kept in mind:

- Maintain a healthy weight.
- Be physically active.
- Eat a diet rich in whole grains, vegetables, fruit and beans.
- Limit consumption of ‘fast foods’ and other processed foods high in fat, starches or sugars.
- Limit consumption of red and processed meat.
- Limit consumption of sugar-sweetened drinks.
- Limit alcohol consumption.
- Do not use supplements for cancer prevention.

Primary reference

Unless specifically indicated otherwise, the review refers to: World Cancer Research Fund/American Institute for Cancer Research. Diet, nutrition, physical activity and cancer: A global perspective. Continuous Update Project Expert Report, 2018. Available at: dietandcancerreport.org.

Additional references

Barrubés L, et al. Association between dairy product consumption and colorectal cancer risk in adults: A systematic review and meta-analysis of epidemiologic studies. *Adv Nutr* 2019;10:S190–S211.

Bermejo LM, et al. Milk and dairy product consumption and bladder cancer risk: A systematic review and meta-analysis of observational studies. *Adv Nutr* 2019;10:S224–S238.

El kinany K, et al. Dairy products and colorectal cancer in Middle Eastern and North African countries: A systematic review. *BMC Cancer* 2018;18:233.

López-Plaza B, et al. Fermented dairy foods intake and risk of cancer. *Adv Nutr* 2019;10:S212–S223.

Sargsyan A, Dubasi HB. Milk consumption and prostate cancer: A systematic review. *World J Mens Health* 2020;38:e41.

Sergentanis TN, et al. Meat, fish, dairy products and risk of hematological malignancies in adults – a systematic review and meta-analysis of prospective studies. *Leuk Lymphoma* 2019; 60(8):1978–1990.

Signal V, et al. Dairy consumption and risk of testicular cancer: A systematic review. *Nutr Cancer* 2018;70(5):710–736.

Zhang K, et al. Milk and dairy product consumption and prostate cancer risk and mortality: An overview of systematic reviews and meta-analyses. *Int J Cancer* 2019;144:2099–2108.

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