

**Clinical Question: Brief description of patient problem/setting (summarize the case very briefly)**

48-year-old man comes into urgent care out of concern for rectal bleeding. On physical examination no external or internal hemorrhoids were appreciated. Vital signs remain stable, and the patient is in no acute distress. The patient notes concern for cancer, stating that his father had colorectal cancer. He says that he has been reading online that dairy products can mitigate colorectal cancer. He asks whether he should increase his intake of dairy products as a preventative measure against colorectal cancer.

**PICO Question: Clearly state the question (including outcomes or criteria to be tracked)**

Is the increased use of dairy products associated with decreased rates of colorectal cancer in adults?

**PICO search terms:**

<b>P</b>	<b>I</b>	<b>C</b>	<b>O</b>
Adults	Intake of dairy products	Adenoma or polyp -free	Incidence of colorectal cancer

**Search tools and strategy used:**

Please indicate what data bases/tools you used, provide a list of the terms you searched together in each tool, and how many articles were returned using those terms and filters.

<b>Database</b>	<b>Terms</b>	<b>Filter</b>	<b>Articles</b>
<b>Wiley Online Library</b>	Adult Dairy products Colon polyps Incidence of colorectal cancer	Journals Last 5 Years Full Access	653
<b>Cochrane Library (Wiley)</b>	Adult Dairy products Colon polyps Incidence of colorectal cancer	Last 2 years	15
<b>PubMed</b>	Adult Dairy products Colon polyps Incidence of colorectal cancer	Clinical Trial Review Last 5 Years Humans Free Full Text	16
<b>JAMA</b>	Adult Dairy products Colon polyps Incidence of colorectal cancer	Review Research Case Report	32
<b>ScienceDirect</b>	Adult Dairy products Colon polyps Incidence of colorectal cancer	Last 5 Years Review Articles Open Access	36

**Results found: 752**

**Explain how you narrow your choices to the few selected articles.**

Colorectal cancer remains an area of concern for many individuals in the United States. The link between dairy and colorectal cancer remains an area of extremely focused research. There are limited but strong forms of data available to answer the above PICO question. During my research, I needed to peruse through the results to find those related to the above question. A total of 6 systematic reviews were considered for inclusion. The other articles focused on vitamin D and the DASH diet rather than dairy products alone. The included articles were initially individually selected by assessing the abstract to ensure that they met the criteria of my PICO question. These articles were found from various databases as listed above.

### **Articles Chosen:**

**CITATION** Guo, L. L., Li, Y. T., Yao, J., Wang, L. S., Chen, W. W., He, K. Y., Xiao, L., & Tang, S. H. (2021). Dairy Consumption and Risk of Conventional and Serrated Precursors of Colorectal Cancer: A Systematic Review and Meta-Analysis of Observational Studies. *Journal of oncology*, 2021, 9948814. <https://doi.org/10.1155/2021/9948814>

**ABSTRACT** **Objective:** The consumption of dairy is associated with decreased risk of colorectal cancer (CRC), but few studies have assessed the relationship between dairy consumption and precursors of CRC. Therefore, we performed the first meta-analysis to further evaluate this association.

**Methods:** PubMed, Embase, Scopus, and Web of Science databases were searched through July 2020 for observational studies. Study-specific risk estimates for the highest versus lowest category were pooled using the random-effects and fixed-effects model. The methodological quality of included studies was assessed using the ROBINS-I Scale.

**Results:** A total of 12 studies were included (3 cohort studies and 9 case-control studies). Compared with the lowest level consumption, fermented dairy products had a decreased risk of precursors of CRC in both cohort (RR = 0.92 95% CI: 0.87-0.97) and case-control studies (RR = 0.98 95% CI: 0.96-0.99). Total dairy (RR = 0.80 95% CI: 0.68-0.96) and cheese (RR = 0.96 95% CI: 0.93-0.99) consumption was inversely associated with the risk in case-control studies whereas yogurt consumption was inversely associated with the risk in cohort studies (RR = 0.91 95%CI: 0.86-0.96). No significant associations were found for consumption of total milk and non/low-fat milk. For dose-response analyses, evidence of linear association was found in total dairy and yogurt consumption. The risk decreased by 12% for an increment of 200 g/d total dairy consumption (RR = 0.88 95% CI: 0.81-0.95) and decreased by 8% for an increment of 50 g/d yogurt consumption (RR = 0.92 95% CI: 0.85-0.99).

**Conclusions:** Fermented dairy products, specifically yogurt and cheese, were significantly associated with decreased risk of conventional and serrated precursors of colorectal cancer.

**LINK/PDF** <https://pubmed.ncbi.nlm.nih.gov/34122548/>

**CITATION** Emami, M. H., Salehi, M., Hassanzadeh Keshteli, A., Mansourian, M., Mohammadzadeh, S., & Maghool, F. (2021). Calcium and dairy products in the

chemoprevention of colorectal adenomas: a systematic review and meta-analysis. *Critical reviews in food science and nutrition*, 1–25. Advance online publication. <https://doi.org/10.1080/10408398.2021.1911927>

**ABSTRACT** The risk of transition to colorectal cancer (CRC) in advanced colorectal adenomas (ACAs) is about 2.5 times higher than the non-advanced ones. This systematic review and meta-analysis was performed to determine the effect of calcium and dairy products on the incidence of CAs and ACAs. Six databases were systematically searched and 37 relevant clinical trials and observational studies involving over 10,964 cases were selected for inclusion. The results showed that calcium consumption reduced the risk of CAs incidence by 8% (RR: 0.92; 95% CI: 0.89-0.96), and calcium intake as a food and dairy product reduced it about 21% (RR: 0.79; 95% CI: 0.72-0.86), and 12% (RR: 0.88; 95% CI: 0.78-0.98), respectively. However, calcium supplementation did not show a significant effect on CAs incidence (RR: 0.97; 95% CI: 0.89-1.05). Results also revealed that total calcium intake markedly reduced the risk of ACAs (RR: 0.79; 95% CI: 0.73-0.85) and the risk of recurrence of adenomas about 12% (RR: 0.88; 95% CI: 0.84-0.93). Our results suggest that natural sources of calcium such as dairy products and foods may have more effective role than supplementary calcium in terms of reducing the risk of incidence and recurrence of colorectal adenomas and advanced adenomas.

**LINK/PDF** <https://pubmed.ncbi.nlm.nih.gov/33951958/>

**CITATION** Barrubés, L., Babio, N., Becerra-Tomás, N., Rosique-Esteban, N., & Salas-Salvadó, J. (2019). Association Between Dairy Product Consumption and Colorectal Cancer Risk in Adults: A Systematic Review and Meta-Analysis of Epidemiologic Studies. *Advances in nutrition (Bethesda, Md.)*, 10(suppl\_2), S190–S211. <https://doi.org/10.1093/advances/nmy114>

**ABSTRACT** Dairy product consumption may decrease colorectal cancer (CRC) risk, but very few studies have evaluated the association between different types of dairy products and CRC location. The aim of this systematic review and meta-analysis was to examine the associations between dairy product consumption and CRC incidence. Summary RRs and ORs with 95% CIs were estimated. A total of 15 cohort studies and 14 case-control studies comprising a total of >22,000 cases were included in the quantitative synthesis. The cohort studies showed a consistent significant decrease in CRC risk associated with higher consumption of total dairy products (RR: 0.80; 95% CI: 0.70, 0.91) and total milk (RR: 0.82; 95% CI: 0.76, 0.88) compared with the CRC risk associated with lower consumption. These studies also showed a significant protective association between low-fat milk consumption and CRC (RR: 0.76; 95% CI: 0.66, 0.88), but only for colon cancer (RR: 0.73; 95% CI: 0.61, 0.87). Cheese consumption was inversely associated with the risk of CRC (RR: 0.85; 95% CI: 0.76, 0.96) and proximal colon cancer (RR: 0.74; 95% CI: 0.60, 0.91). No significant associations with CRC were found for the consumption of low-fat dairy products, whole milk, fermented dairy products, or cultured milk. Most of these associations were not supported by the case-control studies. In

conclusion, high consumption of total dairy products and total milk was associated with a lower risk of developing CRC at any anatomic location, including the proximal and distal colon and the rectum. Low-fat milk consumption was associated with a lower risk of CRC, but this association was restricted to colon cancer. Cheese consumption was associated with the prevention of CRC, specifically proximal colon cancer. Further studies on larger samples and with longer follow-up periods, along with appropriately designed and executed clinical trials, are warranted to determine whether dairy product consumption affects CRC development.

**LINK/PDF** <https://pubmed.ncbi.nlm.nih.gov/31089733/>

**CITATION** Vieira, A. R., Abar, L., Chan, D., Vingeliene, S., Polemiti, E., Stevens, C., Greenwood, D., & Norat, T. (2017). Foods and beverages and colorectal cancer risk: a systematic review and meta-analysis of cohort studies, an update of the evidence of the WCRF-AICR Continuous Update Project. *Annals of oncology : official journal of the European Society for Medical Oncology*, 28(8), 1788–1802. <https://doi.org/10.1093/annonc/mdx171>

**ABSTRACT** **Objective:** As part of the World Cancer Research Fund International Continuous Update Project, we updated the systematic review and meta-analysis of prospective studies to quantify the dose-response between foods and beverages intake and colorectal cancer risk.

**Data sources:** PubMed and several databases up to 31 May 2015.

**Study selection:** Prospective studies reporting adjusted relative risk estimates for the association of specific food groups and beverages and risk of colorectal, colon and rectal cancer.

**Data synthesis:** Dose-response meta-analyses using random effect models to estimate summary relative risks (RRs).

**Results:** About 400 individual study estimates from 111 unique cohort studies were included. Overall, the risk increase of colorectal cancer is 12% for each 100 g/day increase of red and processed meat intake (95% CI = 4-21%, I<sup>2</sup>=70%, pheterogeneity (ph)<0.01) and 7% for 10 g/day increase of ethanol intake in alcoholic drinks (95% CI = 5-9%, I<sup>2</sup>=25%, ph = 0.21). Colorectal cancer risk decrease in 17% for each 90g/day increase of whole grains (95% CI = 11-21%, I<sup>2</sup> = 0%, ph = 0.30, 6 studies) and 13% for each 400 g/day increase of dairy products intake (95% CI = 10-17%, I<sup>2</sup> = 18%, ph = 0.27, 10 studies). Inverse associations were also observed for vegetables intake (RR per 100 g/day =0.98 (95% CI = 0.96-0.99, I<sup>2</sup>=0%, ph = 0.48, 11 studies) and for fish intake (RR for 100 g/day = 0.89 (95% CI = 0.80-0.99, I<sup>2</sup>=0%, ph = 0.52, 11 studies), that were weak for vegetables and driven by one study for fish. Intakes of fruits, coffee, tea, cheese, poultry and legumes were not associated with colorectal cancer risk.

**Conclusions:** Our results reinforce the evidence that high intake of red and processed meat and alcohol increase the risk of colorectal cancer. Milk and

whole grains may have a protective role against colorectal cancer. The evidence for vegetables and fish was less convincing.

**LINK/PDF** <https://pubmed.ncbi.nlm.nih.gov/28407090/>

**CITATION** Schwingshackl, L., Schwedhelm, C., Hoffmann, G., Knüppel, S., Laure Preterre, A., Iqbal, K., Bechthold, A., De Henauw, S., Michels, N., Devleesschauwer, B., Boeing, H., & Schlesinger, S. (2018). Food groups and risk of colorectal cancer. *International journal of cancer*, 142(9), 1748–1758.  
<https://doi.org/10.1002/ijc.31198>

**ABSTRACT** The aim of this systematic review and meta-analysis was to summarize the evidence on the relationship between intake of 12 major food groups, including whole grains, refined grains, vegetables, fruit, nuts, legumes, eggs, dairy, fish, red meat, processed meat and sugar-sweetened beverages with risk of colorectal cancer (CRC). We conducted a systematic search in PubMed and Embase for prospective studies investigating the association between these 12 food groups and risk of CRC until April 2017. Summary risk ratios (RRs) and 95% confidence intervals (95% CI) were estimated using a random effects model for high vs. low intake categories, as well as for linear and nonlinear relationships. An inverse association was observed for whole grains (RR<sub>30g/d</sub> : 0.95, 95% CI 0.93, 0.97; n = 9 studies), vegetables (RR<sub>100g/d</sub> : 0.97, 95% CI 0.96, 0.98; n = 15), fruit (RR<sub>100g/d</sub> : 0.97, 95% CI 0.95, 0.99; n = 16) and dairy (RR<sub>200g/d</sub> : 0.93, 95% CI 0.91, 0.94; n = 15), while a positive association for red meat (RR<sub>100g/d</sub> : 1.12, 95% CI 1.06, 1.19; n = 21) and processed meat (RR<sub>50g/d</sub> : 1.17, 95% CI 1.10, 1.23; n = 16), was seen in the linear dose-response meta-analysis. Some evidence for nonlinear relationships was observed between vegetables, fruit and dairy and risk of colorectal cancer. Findings of this meta-analysis showed that a diet characterized by high intake of whole grains, vegetables, fruit and dairy products and low amounts of red meat and processed meat was associated with lower risk of CRC.

**LINK/PDF** <https://pubmed.ncbi.nlm.nih.gov/29210053/>

**CITATION** Ralston, R. A., Truby, H., Palermo, C. E., & Walker, K. Z. (2014). Colorectal cancer and nonfermented milk, solid cheese, and fermented milk consumption: a systematic review and meta-analysis of prospective studies. *Critical reviews in food science and nutrition*, 54(9), 1167–1179.  
<https://doi.org/10.1080/10408398.2011.629353>

**ABSTRACT** Colorectal cancer is the second most prevalent cancer worldwide. A systematic review and meta-analysis of prospective studies was conducted to examine the association between intake of different types of dairy foods during adulthood and the development of colorectal cancer, specifically comparing nonfermented milk, solid cheese, and fermented milk. Seven databases were systematically searched and 15 cohort studies selected for inclusion, involving over 900,000 subjects and over 5200 colorectal cancer cases. Meta-analysis resulted in an

overall relative risk of colon cancer of 0.74 (95% confidence interval 0.60-0.91) in men consuming nonfermented milk (highest intake category averaging 525 g/day). No association was found between consumption of nonfermented milk and rectal cancer in men or nonfermented milk and colon or rectal cancer in women. No protective association was found between consumption of solid cheese or fermented milk and colorectal cancer. Reasons for the differences in the impact of nonfermented milk, solid cheese, and fermented milk in the colon are discussed. This meta-analysis supports the inverse association between nonfermented milk consumption and risk of colon cancer in men, and provides an evidence base to assist in the formulation of dietary guidelines involving dairy foods.

**LINK/PDF** <https://pubmed.ncbi.nlm.nih.gov/24499149/>

**Summary of the Evidence:**

<b>Author (Date)</b>	<b>Level of Evidence</b>	<b>Sample/Setting (# of subjects/studies, cohort definition etc)</b>	<b>Outcome(s) studied</b>	<b>Key Findings</b>	<b>Limitations and Biases</b>
Guo, L. L., Li, Y. T., Yao, J., Wang, L. S., Chen, W. W., He, K. Y., Xiao, L., & Tang, S. H. (2021)	Systematic review	Searched PubMed, Embase, Scopus, and Web of Science database in English until April 2020 Subgroup analyses were performed according to study design, geographic location, patient sex, number of cases, size of adenoma, type of colorectal lesion, study quality, and type of food frequency questionnaire  1377 potentially relevant articles were initially retrieved, 563 duplicate articles were excluded, and 58 articles	Highest Consumption Compared with Lowest Consumption Analysis Conducted subgroup and sensitivity analyses to explore the sources of heterogeneity Effect of the following on the likelihood of colorectal adenomas and serrated lesions <ul style="list-style-type: none"> <li>total dairy consumption</li> <li>total milk consumption</li> <li>non/low-fat milk consumption</li> </ul>	Intake of total dairy, fermented dairy products, yogurt, and cheese was significantly associated with a decreased risk of colorectal adenomas and serrated lesions  Trend meta-analysis showed a significant negative dose-response relationship in total dairy (P–nonlinearity = 0.947) and yogurt (P–nonlinearity = 0.794) consumption from linearity.  200 gram per day of total dairy consumption could decrease 12% risk	Small number of included studies and subjects  Few of the included studies reported dose related response of dairy products  Most of the case-control studies might not have avoided

		<p>remained for full-text review, a total of 12 eligible articles were included, 9 case-control and 3 cohort studies</p> <p>Quality of 12 included studies was evaluated to have a moderate risk of bias by ROBINS-I tool</p>	<ul style="list-style-type: none"> <li>• fermented dairy product consumption</li> <li>• yogurt consumption</li> <li>• cheese consumption</li> </ul> <p>Linear and nonlinear dose-response analyses</p>	<p>of colorectal adenomas and serrated lesions as indicated by a fixed effect model with no heterogeneity (RR = 0.88, 95%CI: 0.81–0.95, P = 0.001; Ph = 0.658)</p> <p>Risk of colorectal adenomas and serrated lesions decreased by 8% with a daily increment of 50 grams yogurt using the fixed-effect model (RR = 0.92, 95% CI: 0.85–0.99, P = 0.037; Ph = 0.367)</p> <p><b>Total dairy consumption:</b> significantly negative association was observed among overall studies (RR = 0.80 95% CI: 0.69–0.93, P = 0.003; I<sup>2</sup> = 4.6%)</p> <p><b>Total milk consumption:</b> pooled summary effect size indicated no significant association in overall studies (RR = 1.00 95% CI: 0.88–1.13, P = 0.983; I<sup>2</sup> = 32.4%)</p>	<p>the dietary recall bias</p> <p>Dietary behavior is often associated by other factors which were not in consideration such as wealth, exercise, smoking, drinking alcohol, and obesity</p>
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				<p><b>Non/low-fat milk consumption:</b> significant association was observed among overall studies (RR =0.96 95% CI: 0.81-1.14, P= 0.659; I<sup>2</sup> = 0%)</p> <p><b>Fermented dairy product consumption:</b> significantly negative association was observed among overall studies (RR = 0.97 95%CI: 0.96-0.99, P ≤ 0.001; I<sup>2</sup> = 41.9%)</p> <p><b>Yogurt consumption:</b> negative association was observed among overall studies (RR =0.93 95% CI: 0.87-0.99, P = 0.029; I<sup>2</sup> = 50.2%)</p> <p><b>Cheese consumption:</b> negatively associated among overall studies (RR = 0.96 95% CI: 0.93-0.99, P = 0.017; I<sup>2</sup> = 0%)</p>	
Emami, M. H., Salehi, M., Hassanzadeh Keshteli, A., Mansourian, M.,	Systematic review	Searched electronic databases including Scopus, PubMed, Coherence library, EMBASE, Web of Science and	Risk of colorectal adenoma, advanced adenoma, recurrence adenoma Subgroup analysis was	Calcium intake as a food, significantly reduces the risk of adenoma about 21% (RR: 0.79; 95% CI: 0.72-0.86), and as a	Possibility of bias publication Only included

<p>Mohammadzadeh, S., &amp; Maghool, F. (2021)</p>		<p>Google scholar up to September 2020 Included studies estimating the relative risk (RR) with 95% confidence intervals (CIs)</p> <p>37 articles including 10964 cases were selected for meta-analysis of them, 21 evaluated the effect of calcium intake (dietary/dairy products/supplementary/total calcium)</p>	<p>performed based on sex for incidence of adenoma and recurrence adenoma</p>	<p>dairy product about 12% (RR: 0.88; 95% CI: 0.78–0.98)</p> <p>Calcium supplementation did not have a significant effect on adenoma incidence (RR: 0.97; 95% CI: 0.89–1.05)</p> <p>Combination of the results showed a significant effect of calcium on reducing advanced adenomas (RR: 0.79; 95% CI: 0.73–0.85) Calcium intake significantly reduces the recurrence adenoma by about 12% (RR: 0.88; 95% CI: 0.84–0.93)</p>	<p>English studies Doses between articles was not uniform</p> <p>Dietary behavior is often associated by other factors which were not in consideration such as wealth, exercise, smoking, drinking alcohol, and obesity</p>
<p>Barrubés, L., Babio, N., Becerra-Tomás, N., Rosique-Esteban, N., &amp; Salas-Salvadó, J. (2019)</p>	<p>Systematic review</p>	<p>29 studies were included in the meta-analysis: 15 prospective cohort studies and 14 case-control studies</p> <p>Cohort studies included 1,371,848 adult participants (66% women, 31% men, and 3% undefined) with 11,733 cases recorded during follow-up periods that ranged from 4 to 14.8 years</p>	<p>Assessed for CRC risk in prospective cohort studies with use of</p> <ul style="list-style-type: none"> <li>• Total dairy products</li> <li>• High-fat dairy products</li> <li>• Low-fat dairy products</li> <li>• Total milk</li> <li>• Whole milk</li> <li>• Low fat milk</li> <li>• Fermented dairy products</li> </ul>	<p><b>Total dairy products:</b> In cohort studies the summary RR for CRC was 0.80 (95% CI: 0.70, 0.91; I<sup>2</sup> = 45%; P-heterogeneity = 0.08). In case control studies the summary OR was 0.87 (95% CI: 0.64, 1.20), with moderate heterogeneity among the studies (I<sup>2</sup> = 52%; P-heterogeneity = 0.08).</p>	<p>Many of the included studies were of observational nature</p> <p>Dietary assessments were self-reported and therefore reliability</p>

			<ul style="list-style-type: none"> <li>• Total yogurt</li> <li>• Cultured milk</li> <li>• Cheese</li> </ul> <p>Assessed for CRC risk in case-control studies with use of</p> <ul style="list-style-type: none"> <li>• Total dairy products</li> <li>• High-fat dairy products</li> <li>• Low-fat dairy products</li> <li>• Total milk products</li> <li>• Total yogurt</li> <li>• Cultured milk</li> <li>• Cheese</li> </ul> <p>Dose related analysis</p>	<p><b>High-fat dairy products:</b> In cohort studies the summary RR for colon cancer was 0.82 (95% CI: 0.62, 1.08; I<sup>2</sup> = 0%; P-heterogeneity = 0.77; n = 3). In case control studies the summary OR for colon cancer was 1.11 (95% CI: 0.90, 1.37), with moderate heterogeneity (I<sup>2</sup> = 53%; P-heterogeneity = 0.06).</p> <p><b>Low-fat dairy products:</b> In cohort studies the overall summary RR for colon cancer was 0.82 (95% CI: 0.62, 1.08; I<sup>2</sup> = 0%; P-heterogeneity = 0.77; n = 3). In case control studies the summary OR for colon cancer was 0.85 (95% CI: 0.71, 1.02; I<sup>2</sup> = 24%; P-heterogeneity = 0.26).</p> <p><b>Total milk:</b> In cohort studies found evidence of a significant inverse association with the summary RR of CRC (summary RR: 0.82; 95% CI:</p>	<p>remains a question .</p> <p>Dietary behavior is often associated by other factors which were not in consideration such as exercise , smoking , drinking alcohol, and obesity</p>
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				<p>0.76, 0.88; I<sup>2</sup> = 2%; P-heterogeneity = 0.42). In case control studies they observed a <b><u>significant inverse association</u></b> (OR: 0.85; 95% CI: 0.73, 0.99) for CRC, with no important heterogeneity (I<sup>2</sup> = 0%; P-heterogeneity = 0.50).</p> <p><b>Whole milk:</b> In cohort studies estimates showed an RR of 0.97 (95% CI: 0.86, 1.09), with moderate heterogeneity among the studies (I<sup>2</sup> = 40%; P-heterogeneity = 0.19). In case control studies the</p> <p><b>Low fat milk:</b> In cohort studies combined RR for CRC for the highest compared with the lowest consumption of low-fat milk (18, 19) was 0.76 (95% CI: 0.66, 0.88; I<sup>2</sup> = 42%; P-heterogeneity = 0.19).</p> <p><b>Fermented dairy products:</b> In cohort studies RR was 0.90 (95% CI: 0.73, 1.11; I<sup>2</sup></p>	
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				<p>= 0%; P-heterogeneity = 1.0).</p> <p><b>Total yogurt:</b> In cohort studies the overall risk of CRC between the groups with the highest and lowest consumption RR was 0.87 (95% CI: 0.79, 0.96; I<sup>2</sup> = 57%; P-heterogeneity = 0.07). In case control studies, the pooled risk estimate for CRC was not significant (OR: 0.92; 95% CI: 0.77, 1.09; I<sup>2</sup> = 0%; P-heterogeneity = 0.60).</p> <p><b>Cultured milk:</b> In cohort studies e summary RR was 0.92 (95% CI: 0.79, 1.07; I<sup>2</sup> = 69%; P-heterogeneity = 0.07).</p> <p><b>Cheese:</b> In cohort studies pooled RR was 0.85 (95% CI: 0.76, 0.96), with no significant heterogeneity between the studies (I<sup>2</sup> = 27%; P-heterogeneity = 0.25). In case control studies the OR was 0.95 (95% CI: 0.79, 1.14; I<sup>2</sup> = 0%; P-</p>	
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				<p>heterogeneity = 0.62).</p> <p><b>Dose related analyses:</b>  For <b>total dairy products</b> inverse association was significant for colon cancer (RR: 0.91; 95% CI: 0.88, 0.95; P &lt; 0.001). For <b>total milk</b> there was also a significant linear association for colon cancer (RR: 0.88; 95% CI: 0.84, 0.93; P &lt; 0.001). For <b>total yogurt</b> the combined linear RR for CRC for an increment of one serving of yogurt was 0.72 (95% CI: 0.47, 1.10; P = 0.128). For <b>cheese</b> there was significant linear RR for CRC per 1 serving increment of cheese (RR: 0.93; 95% CI: 0.88, 0.98; P = 0.006).</p>	
<p>Vieira, A. R., Abar, L., Chan, D., Vingeliene, S., Polemiti, E., Stevens, C., Greenwood, D., &amp; Norat, T. (2017)</p>	<p>Systematic review</p>	<p>All the relevant studies were identified by PubMed search, included studies from January 2006 up to May 2015</p> <p>45 dose-response meta-analyses on 15 different foods or food groups using 400 individual study</p>	<p>Assessed affects of nutrition including total dairy products and milk as a risk factor for colorectal cancer through risk assessment and subgroup analyses.</p>	<p>Increased intake of dairy products was associated with a decreased risk of colorectal cancer (RR for 400 g/day =0.87 (95% CI = 0.83–0.90, I<sup>2</sup> = 18%, ph= 0.27, 10 studies)</p> <p>An increase of 200 g/day of milk intake was associated with a</p>	<p>Varied heterogeneity in analyses</p> <p>Some studies did not use a validated food-frequency questionnaire</p>

		<p>estimates from 111 unique cohort studies were included</p> <p>The median number of studies for each meta-analysis was 9 studies (ranging from 4 to 23 studies), with a median number of cases of 6662 per study.</p>		<p>decreased risk of colorectal (RR ¼ 0.94 (95% CI ¼ 0.92–0.96, I 2 ¼ 40%, 0.97, 9 studies)</p> <p>Association of milk intake with colorectal and colon cancer was significant in men, but not in women.</p>	<p>Dietary behavior is often associated by other factors which were not in consideration such as exercise, smoking, drinking alcohol, and obesity</p>
<p>Schwingshackle, L., Schwedhelm, C., Hoffmann, G., Knüppel, S., Laure Preterre, A., Iqbal, K., Bechthold, A., De Henauw, S., Michels, N., Devleesschaauer, B., Boeing, H., &amp; Schlesinger, S. (2018)</p>	<p>Systematic Review</p>	<p>PubMed and Embase were searched for prospective studies until April 2017</p> <p>Of 6,365 articles found, 129 full text articles were assessed. Regarding dairy consumption eighteen studies with 16,910 CRC cases were included</p>	<p>Compared highest to the lowest intake category meta-analysis (overall intake range: 0–1,700 g/d).</p> <p>Subgroup analyses</p>	<p>A strong inverse association was observed (RR: 0.83; 95% CI 0.76, 0.89, I 2 56%, p-heterogeneity &lt; 0.001) for the high vs. low, and for each additional daily 200 g of dairy products (RR: 0.93; 95% CI 0.91, 0.94, I 2 50%, p-heterogeneity 50.64, n 515).</p> <p>No significant heterogeneity was observed between the subgroups.</p> <p>Low and high-fat dairy products showed an inverse association for CRC risk</p>	<p>Small sample size for analysis of dairy products as RF for CRC</p> <p>Did not investigate other dairy products such as cheese etc.</p> <p>Dietary behavior is often associated by other factors</p>

				The risk of CRC decreased by approximately 17% with increasing intake of dairy up to roughly 400 g/d	which were not in consideration such as wealth, exercise, smoking, drinking alcohol, and obesity
Ralston, R. A., Truby, H., Palermo, C. E., & Walker, K. Z. (2014)	Systematic review	<p>Searched through pubmed 288 results were found, 179 were excluded while 91 appeared relevant. Of these 91 studies, 19 studies met inclusion criteria.</p> <p>15 co-hort studies were included in the meta-analysis including 919,680 subjects</p> <p>Length of follow-up ranged from five to 24 years</p>	<p>Meta-analysis was performed to examine the association between CRC and intake of non-fermented milks, solid cheeses, and fermented milks</p> <p>RRs of developing CRC in men and women were extracted for each individual study, comparing the lowest versus the highest category of dairy food intake</p> <p>Average consumption of the highest category of intake (g/day) of non-fermented milk, solid cheese, and fermented milk was calculated from the individual studies</p>	<p>Consumption of non-fermented milk was found to have a significant inverse association with risk of CRC; 17 measures of RR, resulted in an overall RR of 0.85 (95% CI 0.77-0.93) in men and women in the highest category of intake (average: 439 g non-fermented milk/day)</p> <p>The RRs of CRC for consumption of solid cheese and fermented milk were 1.11 (95% CI: 0.90-1.36) and 1.01 (95% CI: 0.89-1.15), respectively, indicating no association.</p>	<p>Older systematic review</p> <p>Possibility of publication bias in selected studies</p> <p>Not enough data points to sufficiently analyze gender and colorectal subsite separately</p>

## **Conclusion(s):**

- Briefly summarize the conclusions of each article, then provide an overarching conclusion.

**Guo, L. L., Li, Y. T., Yao, J., Wang, L. S., Chen, W. W., He, K. Y., Xiao, L., & Tang, S. H. (2021):** There is an inverse association between fermented dairy products (including yogurt and cheese) with the risk of conventional adenomas and serrated lesions. Fermented dairy products intake showed a decreased trend in both cohort and case-control studies but cheese and yogurt consumption display an inverse association only in case-control studies or cohort studies. No significant associations were found for the consumption of total milk and non/low-fat milk. Overall, certain dairy products, particularly fermented dairy products, decreased the risk of colorectal cancer.

**Barrubés, L., Babio, N., Becerra-Tomás, N., Rosique-Esteban, N., & Salas-Salvadó, J. (2019):** There is an association between a higher consumption of total dairy products/total milk and a consistently significant decreased risk of colorectal cancer across all colorectal cancer subsites. High low-fat milk and cheese consumption was also associated with a decreased risk of colorectal cancer. Overall, increasing consumption of dairy products, particularly fermented ones like cheese led to decreased incidences of colorectal cancer.

**Emami, M. H., Salehi, M., Hassanzadeh Keshteli, A., Mansourian, M., Mohammadzadeh, S., & Maghool, F. (2021):** Researchers observed reduction of risk in CAs regardless of the source of calcium, however supplementary use of calcium showed no significant protective effect on the risk of colorectal adenomas. Overall, there is a decreased risk of cancer incidence with dairy consumption regardless of the type of dairy consumed. This was also evidenced by the above article by Guo Et al.

**Schwingshackl, L., Schwedhelm, C., Hoffmann, G., Knüppel, S., Laure Preterre, A., Iqbal, K., Bechthold, A., De Henauw, S., Michels, N., Devleesschauwer, B., Boeing, H., & Schlesinger, S. (2018):** Both low and high-fat dairy products showed an inverse association for CRC risk. Low-fat dairy was associated with a 20–25% decreased risk of CRC. As indicated in the systematic review by Barrubés et al, low fat dairy products are more protective. Overall, the results of this systematic review are indicative of an inverse relationship between dairy consumption and incidence of colorectal cancer.

**Vieira, A. R., Abar, L., Chan, D., Vingeliene, S., Polemiti, E., Stevens, C., Greenwood, D., & Norat, T. (2017):** Moderate to high intake of dairy products was associated with a decreased risk of colorectal cancer. An increase of just 200 mg/day of dairy was a strong form of prevention. Overall increases in dairy consumption are inversely associated with instances of colorectal cancer. These conclusions are similar to the above 4 systematic reviews.

**Ralston, R. A., Truby, H., Palermo, C. E., & Walker, K. Z. (2014):** Consumption of non-fermented milk was associated with a 15% reduced risk of colon cancer in men. No association was found between risk of CRC and consumption of solid cheese or fermented milk. This is an older systematic review which also signifies the negative association between dairy consumption and incidence of colorectal cancer. However, unlike the above 5 systematic reviews, the researchers here did not identify a strong inverse relationship between fermented products like yogurts and cheese. Overall, there was a more significant association with the consumption of non-fermented dairy products.

## **Clinical Bottom Line:**

*Please include an assessment of the following:*

- *Weight of the evidence – summarize the weaknesses/strengths of the articles and explain how they factored into your clinical bottom line (this may recap what you discussed in the criteria for choosing the articles)*

- *Magnitude of any effects*

- *Clinical significance (not just statistical significance)*

- *Any other considerations important in weighing this evidence to guide practice - If the evidence you retrieved was not enough to conclude an answer to the question, **discuss what aspects still need to be explored and what the next studies will have to answer/provide (e.g. larger number, higher level of evidence, answer which sub-group benefits, etc)***

### **PICO Question:**

Is the increased use of dairy products associated with decreased rates of colorectal cancer in adults?

### **Clinical Bottom Line:**

There is an inverse association with the intake of dairy products and the risk of developing colorectal cancer. Some data indicates that increased consumption of dairy can also decrease the risk of CRC. More current research indicates a stronger negative correlation between intake of fermented dairy products and the development of colorectal cancer.

### **Weight of the Evidence** (With Rank (**bolded number**) and Explanation):

1. **Guo, L. L., Li, Y. T., Yao, J., Wang, L. S., Chen, W. W., He, K. Y., Xiao, L., & Tang, S. H. (2021)**: This article was ranked first because it is a very recent systematic review of 9 case-control and 3 cohort studies. It investigated a variety of dairy products and categorized their effects on the development of CRC.
2. **Barrubés, L., Babio, N., Becerra-Tomás, N., Rosique-Esteban, N., & Salas-Salvadó, J. (2019)**: This article was ranked second because it was a systematic review of 27 articles including 1,371,848 adult participants. Due to being a relatively older article It was ranked below the Guo et al article. It also investigated a variety of dairy products and categorized their effects on the development of CRC.
3. **Emami, M. H., Salehi, M., Hassanzadeh Keshteli, A., Mansourian, M., Mohammadzadeh, S., & Maghool, F. (2021)**: This article was ranked third because it was a systematic review of 37 articles including 10964 cases. This paper did not categorize dairy products.
4. **Schwingshackl, L., Schwedhelm, C., Hoffmann, G., Knüppel, S., Laure Preterre, A., Iqbal, K., Bechthold, A., De Henauw, S., Michels, N., Devleeschauwer, B., Boeing, H., & Schlesinger, S. (2018)**: This article was ranked fourth because it was published in 2018. It is a systematic review of 18 studies with 16,910 CRC cases. They did look into low vs high intake of dairy products.
5. **Vieira, A. R., Abar, L., Chan, D., Vingeliene, S., Polemiti, E., Stevens, C., Greenwood, D., & Norat, T. (2017)**: This article was ranked fifth because it was a systematic review of metanalyses. It was published in 2017 and did not categorize dairy products by type.
6. **Ralston, R. A., Truby, H., Palermo, C. E., & Walker, K. Z. (2014)**: This article was ranked sixth because it was the oldest relevant systematic review. It was published in 201 and it investigated fermented and unfermented dairy products.

### **Magnitude of Effects:**

1. **Guo, L. L., Li, Y. T., Yao, J., Wang, L. S., Chen, W. W., He, K. Y., Xiao, L., & Tang, S. H. (2021)**: Significantly negative association of total dairy intake with colorectal adenomas and serrated lesions was observed (RR = 0.80 95% CI: 0.69–0.93, P = 0.003; I<sup>2</sup> = 4.6%).

2. **Barrubés, L., Babio, N., Becerra-Tomás, N., Rosique-Esteban, N., & Salas-Salvadó, J. (2019):** For total yogurt the combined linear RR for CRC for an increment of one serving of yogurt was 0.72 (95% CI: 0.47, 1.10; P = 0.128). For cheese there was significant linear RR for CRC per 1 serving increment of cheese (RR: 0.93; 95% CI: 0.88, 0.98; P = 0.006).
3. **Emami, M. H., Salehi, M., Hassanzadeh Keshteli, A., Mansourian, M., Mohammadzadeh, S., & Maghool, F. (2021):** Calcium intake as a food, significantly reduces the risk of adenoma about 21% (RR: 0.79; 95% CI: 0.72–0.86), and as a dairy product about 12% (RR: 0.88; 95% CI: 0.78–0.98).
4. **Schwingshackl, L., Schwedhelm, C., Hoffmann, G., Knüppel, S., Laure Preterre, A., Iqbal, K., Bechthold, A., De Henauw, S., Michels, N., Devleeschauwer, B., Boeing, H., & Schlesinger, S. (2018):** A strong inverse association was observed (RR: 0.83; 95% CI 0.76, 0.89, I<sup>2</sup> 561%, p-heterogeneity < 0.001) between intake of dairy and CRC.
5. **Vieira, A. R., Abar, L., Chan, D., Vingeliene, S., Polemiti, E., Stevens, C., Greenwood, D., & Norat, T. (2017):** Increased intake of dairy products was associated with a decreased risk of colorectal cancer (RR for 400 g/day =0.87 (95% CI = 0.83–0.90, I<sup>2</sup> = 18%, ph= 0.27, 10 studies).
6. **Ralston, R. A., Truby, H., Palermo, C. E., & Walker, K. Z. (2014):** Significant inverse association with risk of CRC with an overall RR of 0.85 (95% CI 0.77-0.93) in men and women in the highest category of intake (average: 439 g non-fermented milk/day).

### **Clinical Significance:**

Colorectal cancer arises through three major pathways. These pathways are the adenoma-carcinoma sequence, the serrated pathway, and the inflammatory pathway. Dairy products are thought to decrease the risk of colorectal cancer development through a variety of mechanisms that disrupt these aforementioned three pathways. Calcium has been proposed to have an impact on cell proliferation and dairy products are a major source of calcium. Overall, research into the efficacy of dairy products remains somewhat inconclusive. This CAT proposes to investigate the following question. Is increased use of dairy products associated with decreased rates of colorectal cancer in adults? Our patient is concerned about the development of colorectal cancer and is curious about the possible protective effects of dairy products. At this time, I would recommend to the patient to increase his intake of dietary dairy products if there are no significant unwanted adverse effects. As evidenced in the above articles, I would recommend that this patient consume at least 4 servings of dairy products a day, totaling to at least 1200 mg of calcium. As indicated in the systematic review by Vieira et al, at least 400 g/day of dairy was associated with a decreased risk of colorectal cancer. This is equivalent to at least 1.6 cups a day. These recommendations are appropriate if our patient is capable of tolerating lactate in his diet. This can be in the form of milk, yogurt, or cheese. I would prefer that the patient consume yogurt. More recent systematic reviews indicate that there is a significant inverse association between yogurt consumption and incidence of colorectal cancer. Yogurt also offers additional probiotic benefits with proper maintenance of gut microbiota. The overarching conclusion is that increased consumption of dairy products reduces the incidence of colorectal cancer. This is evidenced by all of the above systematic reviews. These articles indicate that within recent years there has been more focused research into the use of dairy products as a preventative measure for colorectal cancer. Older systematic reviews demonstrated that there are inverse associations between dairy product intake and risk of colorectal cancer. More recent systematic reviews indicate that fermented dairy products may provide a stronger benefit in reducing the risk of colorectal cancer.

## **Other Considerations:**

The next step in evaluating the Dose-response analyses of specific types of dairy products are more rigorous and standardized cohort studies followed by systematic reviews and meta-analyses. There is evidence here regarding the potential benefit of dairy products as whole in the prevention of colorectal cancer. As more recent systematic reviews have attempted, there needs to a categorization as to the type of dairy products that might have the most benefit. Also, researchers need to further investigate the role of calcium, as indicated by Emami et al, on the mitigation of colorectal cancer. Further investigation is also needed into the role of vitamin D as well. Researchers also need to consider how other factors such as smoking, alcohol, and obesity might influence dietary behaviors. Such factors are risk factor for colorectal cancer.

## **Sources:**

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