연구 주제

Dataset Used

- Retrospective cohort study on patients diagnosed with CRC
- Contains
    - General patient information (sex, age, education status etc)
    - Dietary intake **1-year prior to diagnosis**

      → can calculate calcium intake
    - Survival data
    - Complication data after surgery

❓ **Questions**

- Data retrieval date (hopefully by next Monday)?
- Duration of data collection?
- Sample size?

1. Dairy Product(→ Calcium Intake) and Colorectal Cancer

Inspired by..

- Shin W-K, Lee H-W, Shin A, Lee J-k, Kang D. Milk Consumption Decreases Risk for Breast Cancer in Korean Women under 50 Years of Age: Results from the Health Examinees Study. *Nutrients*. 2020; 12(1):32. https://doi.org/10.3390/nu12010032

a. Research Questions

- (A) *Does dairy consumption (→calcium intake) decrease risk of mortality in CRC patients?*
- (B) *If so, what is the ideal amount of consumption?*
- (C) *Does the result differ among different dairy product types (→ source of calcium intake)*

  (ex. Should they replace whole milk with skim/low-fat/oat milk?

  Is eating cheese better than milk?

  Is supplemental calcium intake necessary? Or is dietary intake enough/better?)
- (D) *Any interactions with other variables? (ex. More beneficial for women with low vitamin D?)*

b. Background

(1) Risk of development

▼ Jeyaraman MM, Abou-Setta AM, Grant L, *et al.* (2019). airy product consumption and development of cancer: an overview of reviews. *BMJ Open* **9:** e023625.

- an overview of reviews study
- Multiple studies had concluded that dairy consumption is **negatively** correlated with colon cancer **development**.

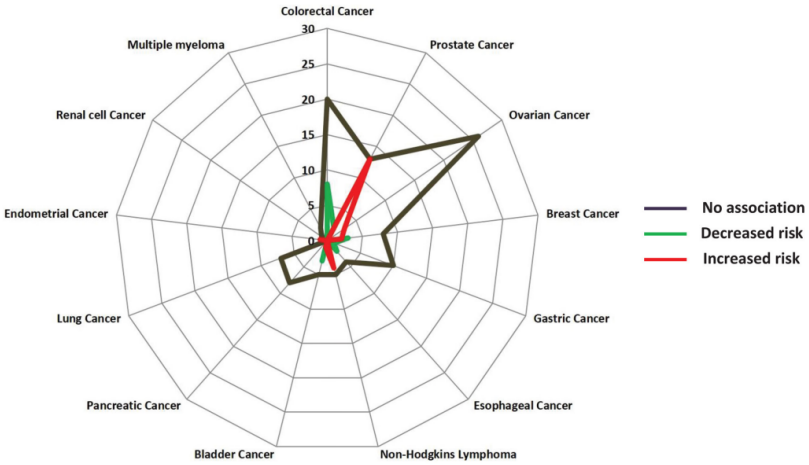


Figure 3 Radar plot depicting the nature of association between dairy consumption and risk of cancer (as reported in included pooled analyses / meta- analyses and systematic reviews (PMASRs)). The numbers on the plot represent the total number of meta-analyses from included PMASRs reporting a specific cancer association. The black, red, and green lines represent number of meta-analyses reporting no association with, increased risk or decreased risk of specific type of cancer, respectively.

Table 2 Nature of association between dairy consumption and risk of cancer reported in included pooled analyses / meta-analyses and systematic reviews

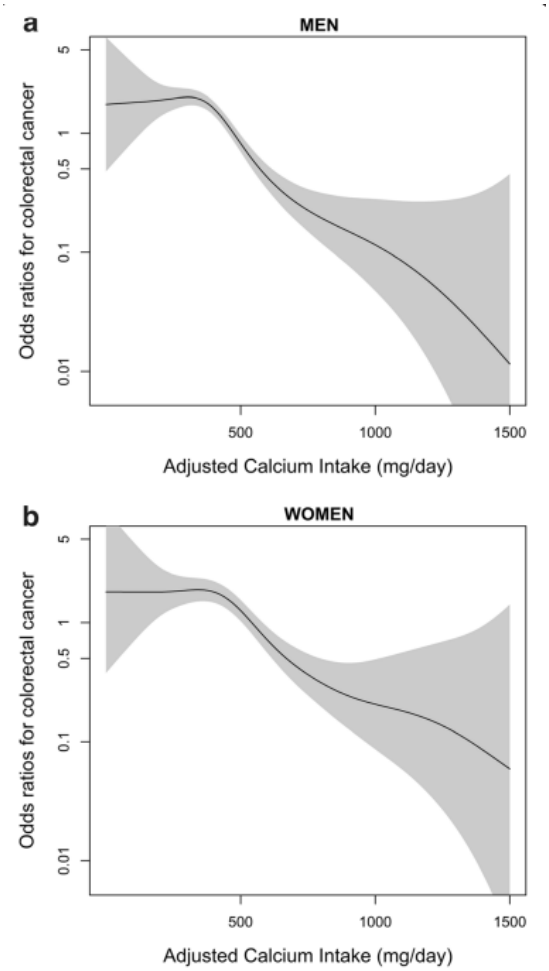
	Type of Cancer													
Type of dairy	CR	PR	OV	BR	GS	EP	NHL	Lung	EM	BL	PN	TD	Renal cell	MM
All dairy products	–	+	∅	∅	∅	∅	∅	∅	+	∅				
	–	+	∅	–	∅	–	+	∅						
	∅	+	∅	∅	∅									
	–∅													
	∅	+												
	–	+												
	∅	∅												
		∅												

▼ Lee, J., Shin, A., Choi, J. Y., Kang, D., & Lee, J. K. (2021). Adherence to the Recommended Intake of Calcium and Colorectal Cancer Risk in the HEXA Study. *Cancer research and treatment*, *53*(1), 140–147

- a community-based prospective cohort study
- Korean women who adhere to the recommended intake of calcium showed a reduced risk of colorectal cancer, but the result was not significant in men.

▼ Han C, Shin A, Lee J, et al. (2015). Dietary calcium intake and the risk of colorectal cancer: a case control study. *BMC Cancer*.15:966.

- Calcium consumption was inversely related to colorectal cancer risk in Korean population where national average calcium intake level is relatively lower than Western countries.
- A decreased risk of colorectal cancer by calcium intake was observed in all sub-sites in men and women.



▼ Zhang, X., Keum, N., Wu, K. et al. (2016). Calcium intake and colorectal cancer risk: Results from the nurses' health study and health professionals follow-up study. *International journal of cancer*, *139*(10), 2232–2242.

- prospective cohort studies (Nurses's Health Study for women, Health Professionals Follow-up Study on men)
- Calcium stimulates differentiation, reduces proliferation, and induces apoptosis.
- Higher calcium intake was associated with a lower risk of developing colon cancer, especially for distal colon cancer.
- **Calcium intake approximately 10 years before diagnosis appeared to be associated with a lower risk of CRC.**

(2) Survival

▼ Yang, W., Ma, Y., Smith-Warner, S. et al. (2019). Calcium Intake and Survival after Colorectal Cancer Diagnosis. *Clinical cancer research : an official journal of the American Association for Cancer Research*, *25* (6), 1980–1988.

- prospective cohort studies (Nurses's Health Study, Health Professionals Follow-up Study)
- Higher calcium intake **after the diagnosis** may be associated with a lower risk of death among patients with colorectal cancer.
- When tested for each type of intake (dietary/supplementary/dairy), the results differed by gender. Supplementary intake was only significant in women, while dietary/dairy intake was only significant in men.
- The effect of pre-diagnostic calcium intake was **not significant**.

▼ Yang B, McCullough ML, Gapstur SM, et al. Calcium, vitamin D, dairy products, and mortality among colorectal cancer survivors: the Cancer Prevention Study-II Nutrition Cohort. *J Clin Oncol*. 2014;32(22):2335-2343.

- a prospective cohort study — cohort consists of patients diagnosed after baseline (1992 or 1993) and up to 2009. Mortality follow-up was through 2010.
- **Higher post-diagnosis intakes of total calcium and milk** may be associated with lower risk of death among patients with nonmetastatic colorectal cancer.
- **Pre-diagnosis** calcium, vitamin D, and dairy product intakes were **not** associated with any mortality outcomes.

> ❗ **Summary**
>
> - Pre-diagnostic calcium intake decreases risk of developing CRC.
> - Post-diagnostic calcium intake increases survival in CRC patients.
> - However, there is yet no evidence that pre-diagnostic calcium intake does the same.

c. Methods

- Logistic regression
- Cox proportional hazards model

Cox Proportional-Hazards Model

The Cox proportional-hazards model (Cox, 1972) is essentially a regression model commonly used statistical in medical research for investigating the association between the survival time of patients and one or more predictor variables.

http://www.sthda.com/english/wiki/cox-proportional-hazards-model

2. Dietary Pattern & Colorectal Cancer

a. Research Questions

- (A) *What are the dietary patterns in CRC patients pre-diagnosis?*
- (B) *Westernized diet was targeted as the main reason for increasing CRC incidence in Korea.*

  → *Is this true? Does it really, compared to Korean traditional diet, contribute to risk of CRC? What about mortality?*

b. Background

- Dietary pattern analysis

Dietary Pattern Analysis

The WCRF/AICR recommendations mainly base on scientific evidence of single exposures. The final question is how well these recommendations perform in combination to reduce cancer risk in the population. One possibility to evaluate the use of the recommendations is to study their association

https://www.sciencedirect.com/topics/food-science/dietary-pattern-analysis

▼ Park Y, Lee J, Oh JH, Shin A, Kim J. Dietary patterns and colorectal cancer risk in a Korean population: A case-control study. *Medicine (Baltimore)*. 2016;95(25):e3759.

- Three dietary patterns (traditional, Westernized, and prudent) were derived by PCA.
- The traditional and prudent patterns were inversely associated with CRC risk, whereas the Westernized pattern showed a positive association, especially among women.

▼ Balakrishna Y, Manda S, Mwambi H, van Graan A. Statistical Methods for the Analysis of Food Composition Databases: A Review. *Nutrients*. 2022;14(11):2193.

▼ Hoang T, Kim H, Kim J. Dietary Intake in Association with All-Cause Mortality and Colorectal Cancer Mortality among Colorectal Cancer Survivors: A Systematic Review and Meta-Analysis of Prospective Studies. *Cancers (Basel)*. 2020;12(11):3391.

▼ Guinter MA, McCullough ML, Gapstur SM, Campbell PT. Associations of Pre- and Postdiagnosis Diet Quality With Risk of Mortality Among Men and Women With Colorectal Cancer [published online ahead of print, 2018 Oct 19]. *J Clin Oncol*. 2018;36(34):JCO1800714.

c. Methods

- For dietary pattern analysis,
  - Reduced rank regression

Reduced Rank Regression - a powerful statistical method for identifying empirical dietary patterns

Reduced Rank Regression - a powerful statistical method for identifying empirical dietary patterns Gina Ambrosini PhD Senior Research Scientist MRC Human Nutrition Research, Cambridge EUCCONET International Workshop, Bristol October 2011. Why dietary patterns ?. Slideshow 2796776 by nantai

https://www.slideserve.com/nantai/reduced-rank-regression-a-powerful-statistical-method-for-identifying-empirical-dietary-patterns

  - PCA
  - Factor analysis
  - K-means clustering
- Cox proportional hazards model