

Yogurt Consumption and Risk of Colorectal Cancer by Anatomic Site of Colon and Calcium Intake: A Meta-Analysis



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INTRODUCTION

- Colorectal cancer (CRC) is the third leading cause of cancer-related death globally¹
- Dietary and lifestyle factors are known to be preventable risk factors that could reduce CRC incidence by 50-60%^{2,3}
- Yogurt contains live microbes that may reshape the gut microbiota, a potential mechanism for its physiological effects⁴
- Yogurt intake tends to be correlated with dairy calcium intake
- As calcium intake appears more strongly associated with distal colon cancer⁵, if the subsite association is different for yogurt, this would provide indirect support of an effect of yogurt that is independent of calcium intake

OBJECTIVES

- To provide updated evidence⁶ about the correlation between yogurt consumption and risk of colorectal cancer (CRC), particularly by CRC anatomical site including proximal and distal colon, as well as rectum
- Additionally, we examined whether the association between yogurt intake and CRC persists after controlling for calcium, a known protective dietary element for CRC

METHODS

Search Strategy:

- A systematic literature search in PubMed, Embase, and Web of Science for studies published up to January 29, 2025

Eligibility Criteria:

- Observational studies or RCTs that compared CRC incidence between yogurt consumers and non-consumers

Data Analysis:

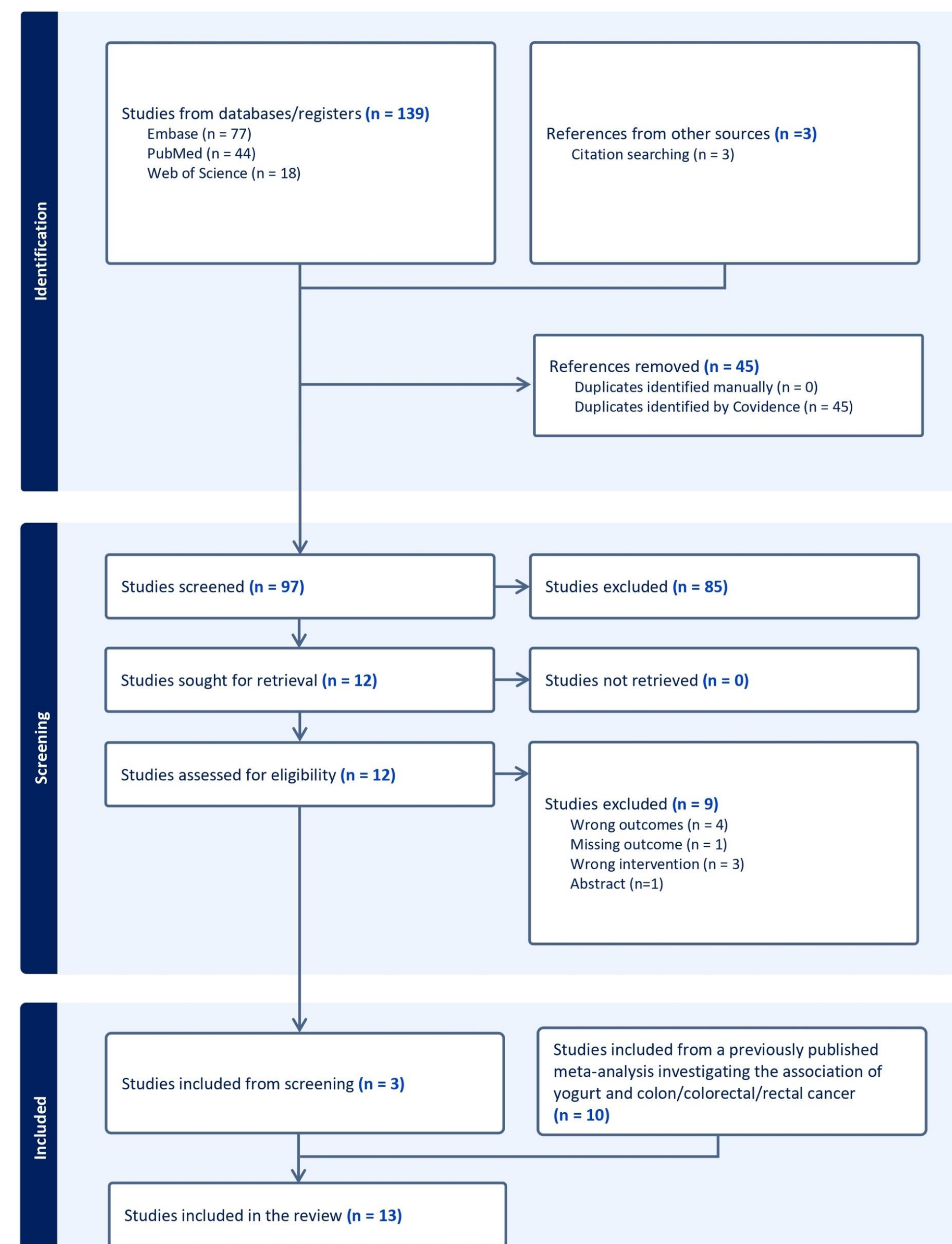
- Effect estimates were pooled using random-effects meta-analysis where heterogeneity was high and fixed-effects otherwise
- Odds Ratios (OR) with 95% Confidence Intervals (CI) were used as the risk estimate
- Subgroup analyses were conducted for CRC anatomical site, sex, study type, publication date, and geographic region
- Additionally, pooled OR for calcium-controlled studies was evaluated
- Publication bias was assessed using funnel plots and Egger's test

CONTACT

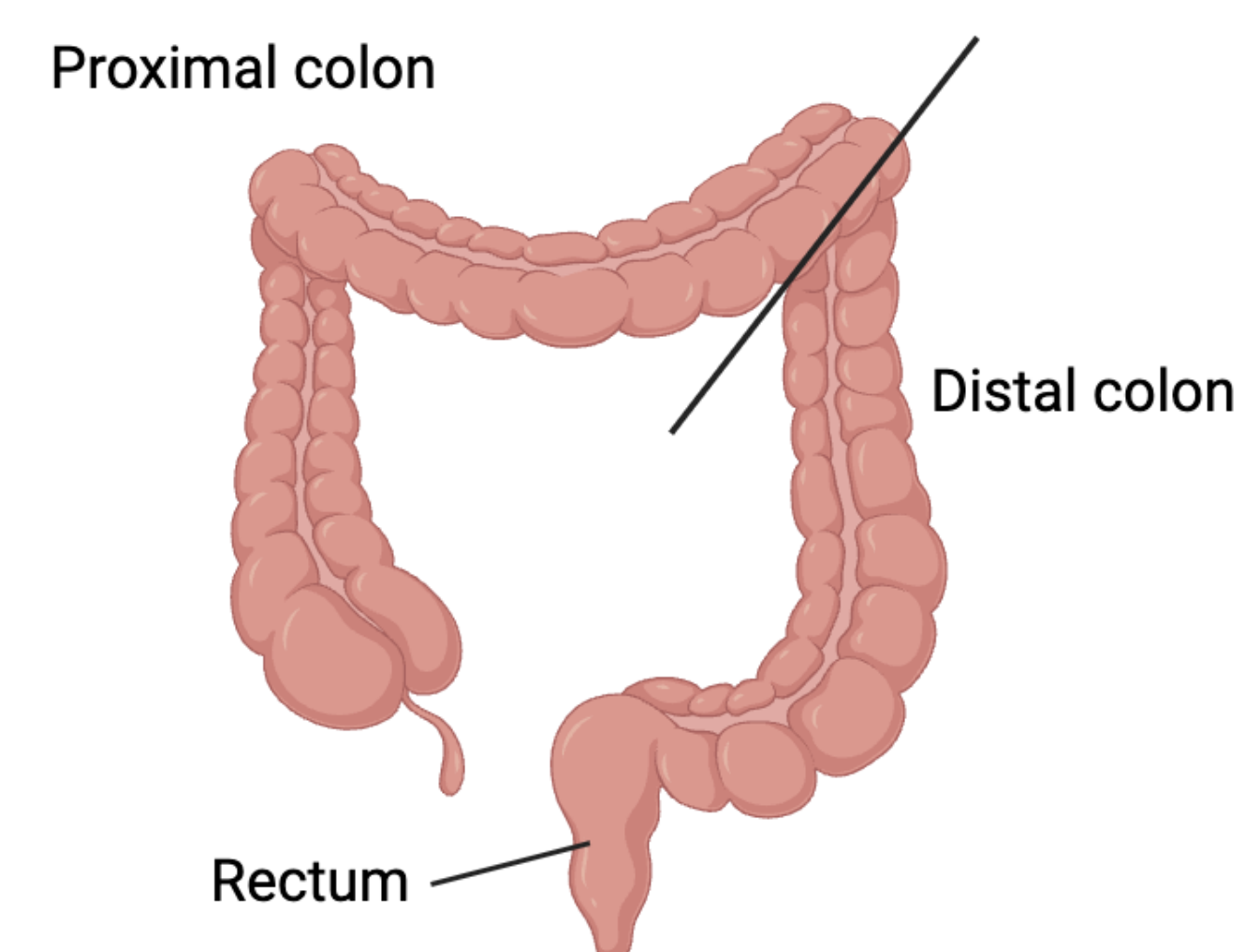
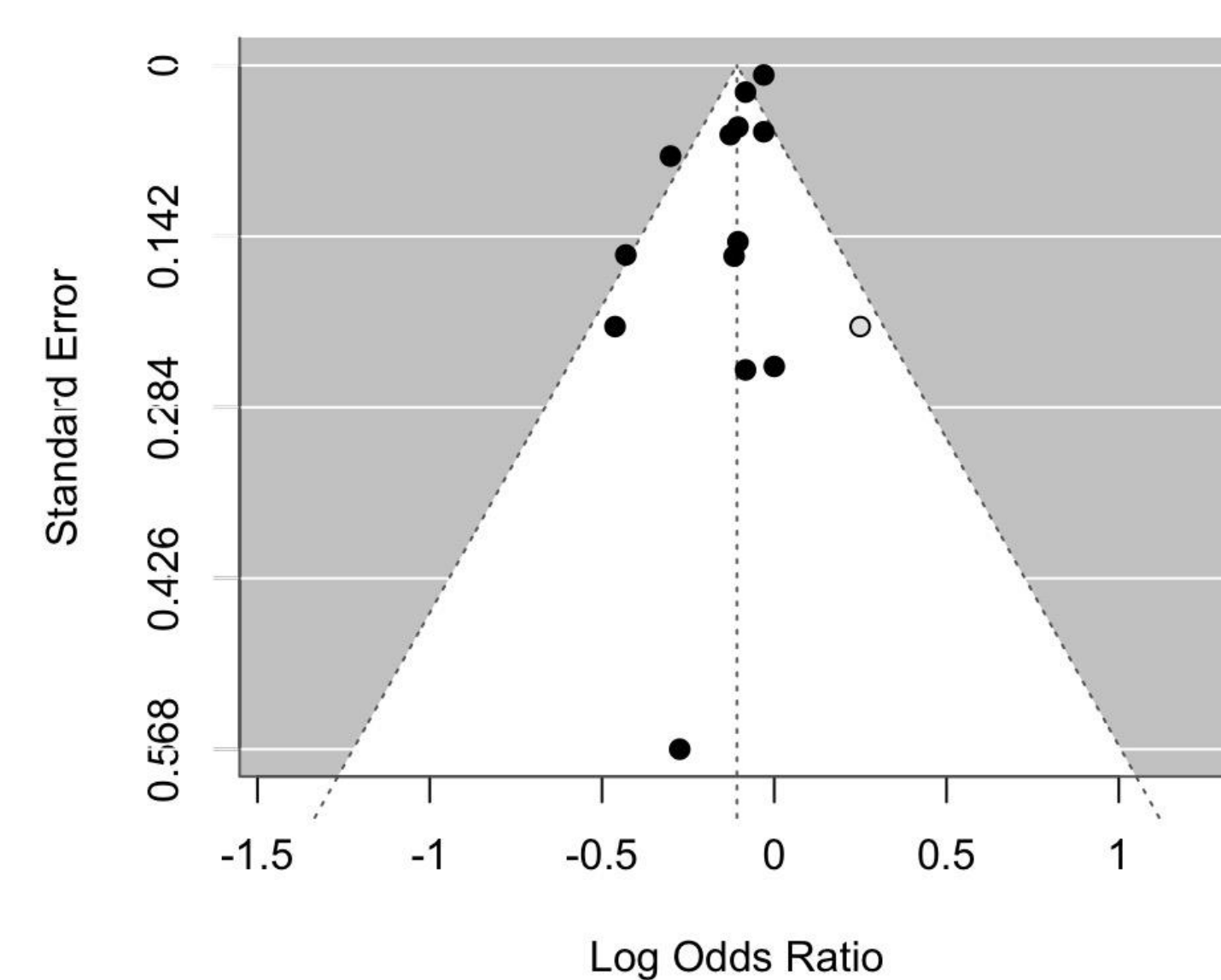
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- Thirteen studies (seven cohort and six case-control) comprising a sample size of 1,312,607 were eligible

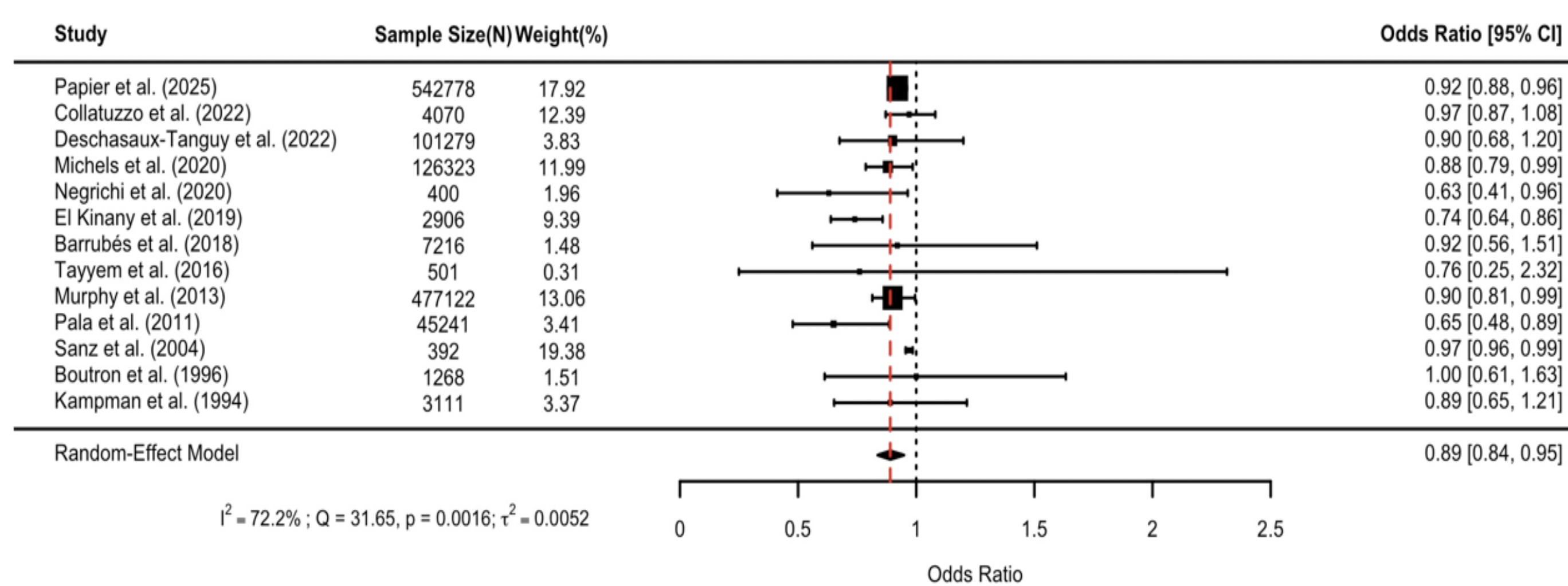


- Funnel plot with trim-and fill method indicating one missing study



RESULTS

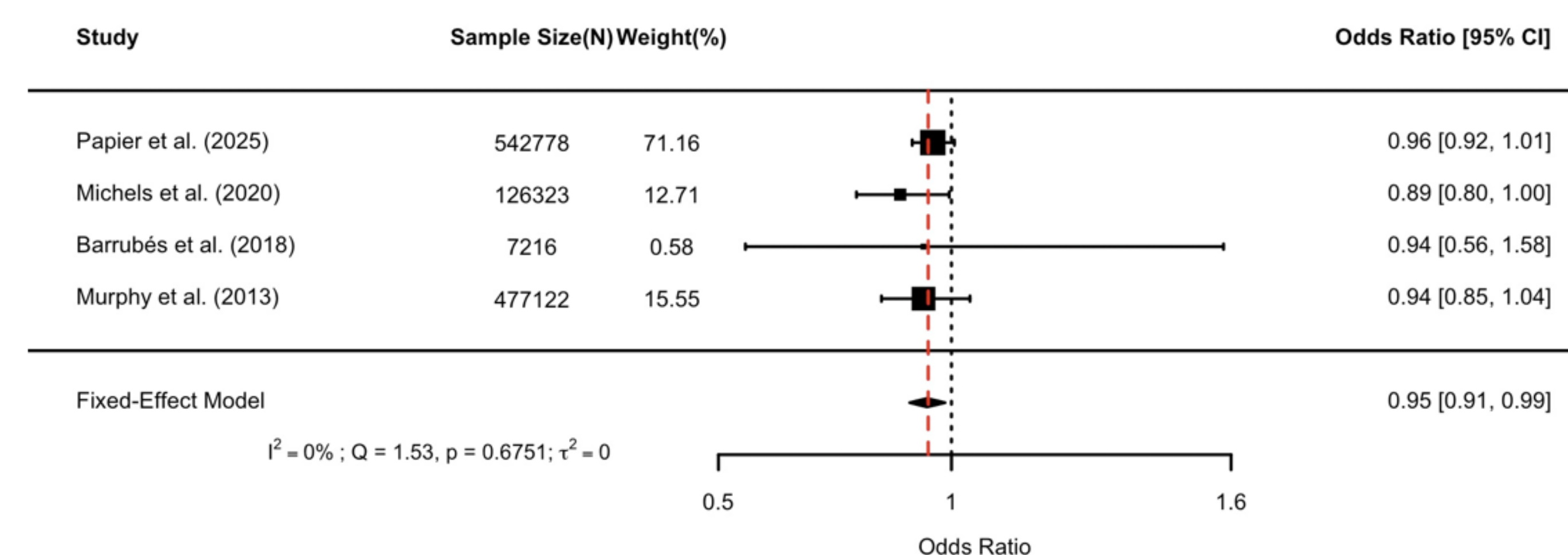
- Yogurt consumption was significantly associated with a lower risk of CRC (OR = 0.89, 95% CI 0.84-0.95)



- Yogurt intake was associated with a slightly lower risk of colon cancer (OR = 0.85, 95% CI 0.79-0.92) than rectal cancer (OR = 0.92, 95% CI 0.86-0.98)
- A slightly lower risk of proximal cancer (OR = 0.86, 95% CI 0.75-0.98) than distal cancer (OR = 0.90, 95% CI 0.84-0.97) associated with yogurt consumption

Calcium consumption

- When controlled for calcium, yogurt consumption showed still significant but weaker association with CRC (OR = 0.95, 95% CI 0.91-0.99) than when not adjusting calcium
- In a difference test of the four studies that reported both models, the pooled ratio of odds ratios for calcium-controlled versus non-controlled analyses was 1.04 (95% CI 0.98-1.10, p = 0.16), indicating no significant difference in effect estimates when calcium was controlled



Subgroup Analysis

| Subgroups | Number of studies | OR (95% CI) | I² |
|-------------------------|-------------------|-------------------|-------|
| Sex | | | |
| Men | 2 | 0.69 (0.36, 1.33) | 82.4% |
| Women | 3 | 0.91 (0.88, 0.95) | 21.6% |
| Study Type | | | |
| Cohort | 7 | 0.91 (0.88, 0.94) | 0% |
| Case-control | 6 | 0.87 (0.75, 1.01) | 79.7% |
| Publication Date | | | |
| Newer (after 2021) | 3 | 0.93 (0.89, 0.96) | 0% |
| Older (before 2021) | 10 | 0.86 (0.78, 0.94) | 68.6% |
| Regions | | | |
| Africa | 2 | 0.73 (0.63, 0.84) | 0% |
| Asia | 2 | 0.97 (0.87, 1.08) | 0% |
| Europe | 8 | 0.93 (0.88, 0.98) | 48.6% |
| North America | 1 | 0.89 (0.80, 1.00) | NA |

DISCUSSION

Main finding:

- The pooled odds ratio <1 indicates a **modest but consistent protective association**
- Protective effects persisted after **adjustment for calcium intake**, suggesting mechanisms **independent of calcium**

Potential biological mechanisms:

- Microbiome-mediated pathways**, particularly relevant to the **proximal colon**
- Yogurt's live cultures (e.g., *Lactobacillus*, *S. thermophilus*) may enhance **short-chain fatty acid (SCFA) production**, **improve barrier function**, and **reduce inflammation**
- Stronger association for proximal colon cancer may reflect **region-specific microbial metabolism** (fermentation occurs mainly in proximal regions)

Subgroup insights:

- Colon vs. rectal cancer:** slightly stronger protective association for colon cancer → supports role of colonic microbiota
- Sex:** significant association in women but not in men
- Geography:** strongest inverse association observed in Africa (small sample sizes warrant caution)
- Study design:** case-control studies showed stronger effects, potentially due to **recall bias**
- Temporal trend:** older studies reported stronger effects, possibly reflecting higher proportion of case-control designs and improvements in dietary assessment over time

Strengths:

- First meta-analysis to examine **CRC subsites** and **independence from calcium intake**

Limitations:

- Publication bias** indicated (Egger's test p<0.05; one potentially missing study)
- Limited number of studies** in some subgroups (e.g., men, Africa, Asia) and **high heterogeneity** in certain analyses

Future directions:

- Conduct **randomized trials** or **prospective cohorts** examining yogurt type, probiotic strains, and dose-response
- Integrate **microbiome analyses** to clarify mechanisms
- Explore **sex-specific** and **population-specific effects** to refine dietary guidelines of CRC

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