

RESEARCH PAPER

FREQUENCY OF RED MEAT AND PROCESSED FOOD CONSUMPTION AND THE OCCURRENCE OF COLORECTAL CANCER IN EAST JAVA, INDONESIA: A MULTICENTRE CASE–CONTROL STUDY

Teuku Harmawansyah^{1*}, Aries Budianto², Dwicha Rahmawansa Siswardana³

^{1,2,3} Department of Surgery, Faculty of Medicine, Universitas Brawijaya / Dr. Saiful Anwar Regional General Hospital, Malang, East Java, Indonesia

***Corresponding Author:** dr. Teuku Harmawansyah, Department of Surgery, Faculty of Medicine, Universitas Brawijaya / Dr. Saiful Anwar Regional General Hospital, Jl. Jaksa Agung Suprpto No. 2, Malang 65112, East Java, Indonesia | Email: teuku.pon92@gmail.com

ABSTRACT

Background: Colorectal cancer (CRC) is the third most commonly diagnosed malignancy worldwide, and its burden is rising in Indonesia. Red and processed meat are established risk factors in Western cohorts, but evidence from Indonesian populations, whose dietary practices differ substantially, remains scarce.

Objective: To determine the association between the frequency of red meat and processed food consumption and CRC occurrence in East Java, Indonesia.

Methods: A multicentre retrospective case–control study was conducted between March and June 2024 at eight sites in East Java. Cases were adults aged 40–70 years with histopathologically confirmed colorectal adenocarcinoma (n = 172); controls were East Java-born adults of the same age range without CRC (n = 175). Consumption frequency (<1, 1 or >1 time/week) was assessed with a culturally adapted food-frequency questionnaire (23 exposure items; Cronbach's $\alpha = 0.907$). Associations were analysed using Pearson's χ^2 , the Mann–Whitney U test and crude odds ratios (ORs) with 95% confidence intervals (CIs).

Results: Red meat consumption frequency was not associated with CRC ($\chi^2 = 2.235$, $p = 0.327$; Mann–Whitney $p = 0.936$). Compared with <1 time/week, ORs were 1.27 (95% CI 0.80–2.04) for once weekly and 0.81 (0.39–1.67) for more than once weekly. Processed food consumption frequency was significantly associated with CRC ($\chi^2 = 8.270$, $p = 0.016$): once-weekly consumption carried an OR of 2.27 (1.26–4.08), whereas consumption more than once weekly yielded an OR of 1.54 (0.70–3.36). No linear trend was observed (linear-by-linear $p = 0.181$). Monthly income differed significantly between groups ($p < 0.001$).

Conclusion: Processed food consumption, but not red meat consumption, was associated with CRC in East Java, although without a consistent dose–response gradient. These crude estimates support dietary counselling to limit processed foods and warrant confirmation in larger studies with quantitative exposure assessment and multivariable adjustment.

Keywords: Colorectal neoplasms; Red meat; Processed foods; Case–control studies; Indonesia

How to cite this article: Harmawansyah T, Budianto A, Efendi A. Frequency of red meat and processed food consumption and the occurrence of colorectal cancer in East Java, Indonesia: a multicentre case–control study. *Int J Drug Deliv Technol*. 2026;16(85s): 510-518; DOI: 10.25258/ijddt.16.85s.48

I. INTRODUCTION

A. Background

Colorectal cancer (CRC) is a malignant neoplasm of the colon or rectum that arises predominantly through a stepwise transformation of normal mucosa into adenoma and subsequently invasive carcinoma. In 2020 it was the third most frequently diagnosed cancer and the second leading cause of cancer death worldwide, with an estimated 1.9 million new cases and 935,000 deaths; the global burden has increased steadily from earlier GLOBOCAN estimates and is projected to rise further by 2035.^{1–3}

Colorectal cancer predominantly affects adults aged 60 years or older and is more frequent in men than in women. Nevertheless, the incidence and mortality of early-onset disease diagnosed before 50 years of age are rising across many regions, including the Asia-Pacific, where mortality from early-onset CRC is disproportionately high among women in Southeast Asia.^{4–10}

In Indonesia, CRC is among the most common malignancies, ranking second in men after lung cancer and fourth in women. Although the age-standardised incidence in Indonesia is lower than in high-income East Asian countries, the country's large population translates into a substantial absolute number of cases, and a considerable proportion of patients present with advanced-stage disease. In East Java, the rising incidence of CRC and ethnically distinct patterns of health-seeking behaviour among the Arek, Mataraman and Pentalungan groups underscore the need for region-specific evidence.^{1,11,12}

Colorectal carcinogenesis results from the accumulation of genetic and epigenetic alterations, including chromosomal instability, microsatellite instability and the CpG island methylator phenotype, that activate oncogenes (e.g., via aberrant Wnt/ β -catenin signalling) and inactivate tumour suppressor genes within a pro-inflammatory tissue microenvironment.^{13–16}

Risk factors for CRC are conventionally classified as non-modifiable—age, sex, hereditary syndromes such as Lynch syndrome and familial adenomatous polyposis, family history and inflammatory bowel disease—and modifiable, including diet, obesity, physical inactivity, smoking and alcohol consumption. Anthropometric factors such as adult height have also been associated with CRC risk. Among modifiable exposures, diets rich in red and processed meat and low in dietary fibre have consistently been linked with an increased risk.^{17–21}

In 2015, the International Agency for Research on Cancer (IARC) classified processed meat as carcinogenic to humans (Group 1) and red meat as probably carcinogenic to humans (Group 2A), largely on the basis of evidence for CRC. The World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) likewise judged the evidence linking processed meat to CRC as convincing. In the European Prospective Investigation into Cancer and Nutrition (EPIC), which followed 478,040 participants, 1,329 incident CRC cases were identified and higher intakes of red and processed meat were associated with increased risk.^{22–25}

Quantitative syntheses have repeatedly confirmed a dose-dependent association. A meta-analysis of prospective studies reported a relative risk of 1.17 per 100 g/day of fresh red meat and 1.18 per 50 g/day of processed meat, and Smolińska and Paluszkiwicz showed that intake of red meat more frequently than once a day or exceeding 50 g/day increased colon cancer risk by approximately 21–37%. More recent pooled analyses of prospective cohorts have reproduced these findings.^{26–30}

Biologically, red and processed meat contain or generate haem iron, N-nitroso compounds, heterocyclic aromatic amines and polycyclic aromatic hydrocarbons, which can induce DNA damage, lipid peroxidation, epithelial hyperproliferation and gut dysbiosis. The magnitude of exposure is determined not only by the amount consumed but also by frequency of consumption,

preservation methods (salting, curing, addition of nitrates or nitrites) and high-temperature cooking.^{18,19,21,31}

B. Research gap

Most of the evidence underpinning current recommendations derives from Western populations. Meta-analyses restricted to East Asian populations have not consistently demonstrated a significant association between red meat intake and CRC, and critical appraisals from an Asian perspective have highlighted that processed meat products, typical portion sizes and cooking methods in Asia differ substantially from those in Europe and North America. Indonesian cuisine is characterised by distinctive red meat preparations (e.g., satay, rawon, rendang, tongseng, gulai and tengkleng) and by a wide range of locally processed foods (e.g., salted fish and instant noodles) in addition to Western-style products. To the best of our knowledge, no study has examined the frequency of red meat and processed food consumption in relation to CRC in the East Java population.^{32–35}

C. Novelty

This study provides the first multicentre case–control evidence from East Java on the association between consumption frequency of red meat and processed foods and CRC. It employed a culturally adapted food-frequency instrument that captures local red meat dishes and a broad, context-specific spectrum of processed foods—Western-style, Middle Eastern-style, locally preserved and canned foods, and processed snacks—rather than relying solely on Western processed meat categories.^{12,33}

D. Objectives

The general objective of this study was to determine the association between the frequency of red meat and processed food dietary patterns and the occurrence of CRC in East Java. The specific objectives were (i) to analyse the association between the frequency of red meat consumption and CRC occurrence, and (ii) to analyse the association between the frequency of processed food consumption and CRC occurrence in East Java.³⁶

E. Hypotheses

The general hypothesis was that the frequency of red meat and processed food dietary patterns is associated with the occurrence of CRC in East Java. The specific hypotheses were: H₁, there is a significant association between the frequency of red meat consumption and CRC occurrence; and H₂, there is a significant association between the frequency of processed food consumption and CRC occurrence in East Java.³⁷

F. Significance of the study

Academically, this study contributes region-specific epidemiological evidence to the fields of nutritional epidemiology and surgical oncology and provides a validated, culturally adapted exposure instrument that may be used in future Indonesian studies. Practically, the findings may inform public-health policy and community education aimed at reducing diet-related CRC risk, support dietary counselling by clinicians, and guide the design of targeted prevention and early-detection programmes in East Java.^{38,39}

II. METHODOLOGY

A. Study design

This was an analytical observational study with a retrospective case–control design, in which patients with CRC (cases) were compared with individuals without CRC (controls) to evaluate the association between prior dietary exposure and disease occurrence. The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations for case–control studies. The conceptual framework is shown in Figure 1.^{36,37}

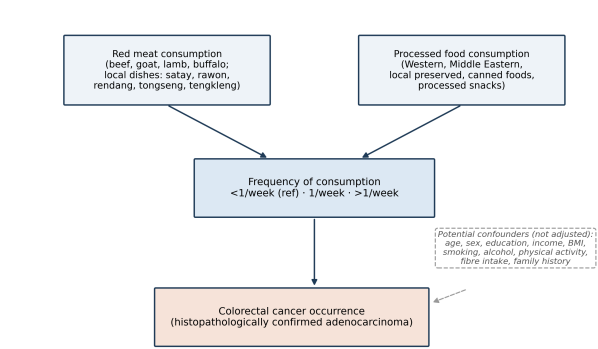


Figure 1. Conceptual framework of the study.

B. Setting and study period

The study was conducted at Dr. Saiful Anwar Regional General Hospital (Malang), Dr. Iskak Regional General Hospital (Tulungagung), DKT Hospital (Jember), the Surabaya Stoma Community, and the private surgical practices of general surgeons in Ngawi, Ponorogo, Bojonegoro and Banyuwangi, East Java, Indonesia. These sites were selected because they are strategically located referral centres with established digestive surgery services delivered by consultant digestive surgeons and receive referrals from surrounding peripheral hospitals, thereby managing a substantial proportion of CRC patients from across the province. Data were collected between March and June 2024.¹²

C. Participants and eligibility criteria

Cases were patients with a histopathologically confirmed diagnosis of colorectal adenocarcinoma, born in East Java and aged 40–70 years. Controls were individuals without a diagnosis of CRC, born in East Java and aged 40–70 years, recruited from the same catchment population as the cases. Exclusion criteria for both groups were a diagnosis of any malignancy other than CRC (e.g., breast, prostate, cervical or ovarian cancer), a history of dementia, and refusal to participate. The exclusion of other malignancies was intended to avoid misattribution of exposure–outcome relationships in patients with synchronous or metachronous cancers.^{37,40}

D. Sampling technique and sample size

A non-probability consecutive sampling technique was used, in which every eligible individual meeting the selection criteria during the study period was recruited until the target sample was reached. In total, 347 participants were enrolled (172 cases and 175 controls), yielding an approximately 1:1 case-to-control ratio.^{36,37}

E. Variables and operational definitions

The independent variables were the frequency of red meat consumption and the frequency of processed food consumption; the dependent variable was CRC status. Red meat was defined as meat that is red in colour and rich in myoglobin and iron (beef, goat, lamb and other meats from four-legged animals), including local preparations. Processed foods were defined as foods or meats that had undergone salting, preservation, canning, fermentation, smoking or industrial preparation. Each exposure was categorised on an ordinal scale as <1 time/week (score 1; reference), 1 time/week (score 2) or >1 time/week (score 3). Operational definitions are summarised in Table 1.^{22,23}

Table 1. Operational definitions of study variables

Variable	Operational definition	Indicator	Categories	Coding	Scale
Red meat	Meat that is red in colour, rich in myoglobin and iron (beef, goat, lamb; other four-legged animals), including satay, empal, rawon, krengsengan, tongseng, rendang, se'i, soto, gulai and tengkleng	Frequency of consumption	<1 time/week; 1 time/week; >1 time/week	1 / 2 / 3	Ordinal

Variable	Operational definition	Indicator	Categories	Coding	Scale
Processed foods	Foods or meats processed by salting, preservation, canning, fermentation, smoking or industrial preparation	Frequency of consumption	<1 time/week; 1 time/week; >1 time/week	1 / 2 / 3	Ordinal
Colorectal cancer	Cancer of the colon or rectum confirmed by clinical, histopathological and/or medical-record data	CRC status	Case; control	CRC / non-CRC	Nominal

F. Research instrument

The instruments were a structured food-frequency questionnaire (FFQ) administered electronically via Google Forms and the medical records of patients with CRC. The FFQ captured usual dietary habits over the preceding three months and contained open- and closed-ended items. The red meat domain comprised 14 items (beef satay, beef empal, beef rawon, beef krengsengan, beef tongseng, beef rendang, beef se'i, beef soto, goat satay, goat curry, goat krengsengan, goat tengkleng, meatballs, and other meats from four-legged animals) and the processed food domain comprised nine items (Western-style foods, Middle Eastern-style foods, local processed foods such as salted fish and instant noodles, canned foods, sweet traditional processed foods, wafers, biscuits, crackers and cookies). The FFQ additionally recorded demographic characteristics (sex, educational attainment and monthly income) and other potential risk factors.^{36,41}

G. Questionnaire development and validation

The questionnaire was developed on the basis of the principles of digestive surgery and current knowledge of CRC risk factors, and content validity was established through review by the research supervisors. A preliminary version was pre-tested among individuals not participating in the main study to identify ambiguous or misleading items; the revised version was then reviewed by a language expert for clarity. Finally, the instrument was pilot-tested in a smaller group with characteristics comparable to those of the target population. Item validity was assessed with Pearson's item–total correlation and internal-consistency reliability with Cronbach's α .^{36,37,41}

H. Data collection procedures

Primary data were obtained through structured interviews and questionnaire completion after written informed consent had been obtained. Secondary data were extracted from the medical records of cases to verify the diagnosis and to obtain tumour location, treatment history and relevant clinical and laboratory findings; histopathological and radiological reports were reviewed to confirm CRC status. The overall study flow is presented in Figure 2.^{42,43}

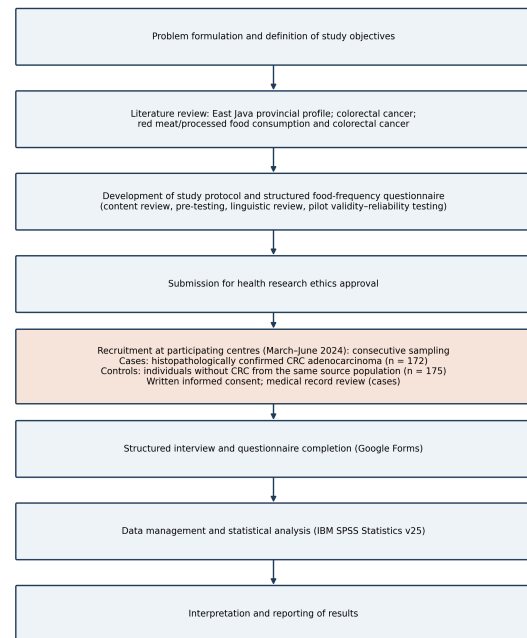


Figure 2. Study flow diagram.

I. Statistical analysis

Univariate analysis described the distribution of participant characteristics and exposure categories. Normality was assessed with the Kolmogorov–Smirnov test ($n > 30$), supplemented by the Shapiro–Wilk test and normal Q–Q plots; because all variables were non-normally distributed ($p < 0.001$), non-parametric methods were applied. Between-group differences in baseline characteristics were compared with Pearson's χ^2 test. Associations between exposure frequency and CRC status were evaluated with Pearson's χ^2 test ($df = 2$), supported by the likelihood-ratio χ^2 and the linear-by-linear association test for trend; the χ^2 assumption was considered satisfied when no more than 20% of cells had an expected count < 5 . The Mann–Whitney U test compared the ordinal distribution of consumption frequency between cases and controls.^{36,37}

The magnitude of association was expressed as crude odds ratios (ORs) with 95% confidence intervals (CIs) calculated by the Woolf (logit) method, using < 1 time/week as the reference category; Wald p-values were derived from the log-OR and its standard error. A supplementary contrast of any consumption of ≥ 1 time/week versus < 1 time/week was computed from the same cross-tabulations. Statistical significance was set at a two-sided α of 0.05. Analyses were performed with IBM SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA).⁴¹

J. Ethical considerations

The study protocol was submitted to and approved by the Health Research Ethics Committee [committee name and approval number to be inserted] prior to data collection, and the study adhered to the principles of the Declaration of Helsinki. All participants provided written informed consent, and data were anonymised before analysis.³⁶

III. RESULTS

A. Characteristics of the study participants

A total of 347 participants were analysed, comprising 175 controls (50.4%) and 172 CRC cases (49.6%). The sex distribution was balanced overall (175 men and 172 women), with a slightly higher proportion of men among cases (54.1%) than among controls (46.9%); this difference was not significant ($p = 0.216$). Senior high school was the most frequent educational attainment (32.3%), followed by elementary school or lower (28.2%),

university (23.1%) and junior high school (16.1%), with no significant difference between groups ($p = 0.459$). The largest income category was $\leq$ IDR 1,900,000 per month (34.0%). Monthly income differed significantly between groups ($\chi^2 = 16.48$, $df = 3$, $p < 0.001$): cases were over-represented in the two lowest income strata (71.5% vs. 52.0% of controls) and under-represented in the highest stratum (9.3% vs. 22.3%) (Table 2).

Table 2. Characteristics of study participants by sex, educational attainment and monthly income ($N = 347$)

Characteristic	Controls (n = 175), n (%)	CRC cases (n = 172), n (%)	Total (N = 347), n (%)	p-value
Sex				0.216
Male	82 (46.9)	93 (54.1)	175 (50.4)	
Female	93 (53.1)	79 (45.9)	172 (49.6)	
Educational attainment				0.459
University	43 (24.6)	37 (21.5)	80 (23.1)	
Senior high school	57 (32.6)	55 (32.0)	112 (32.3)	
Junior high school	23 (13.1)	33 (19.2)	56 (16.1)	
Elementary school or lower	52 (29.7)	46 (26.7)	98 (28.2)	
Monthly income (IDR)				<0.001
>5,000,000	39 (22.3)	16 (9.3)	55 (15.9)	
3,000,001–4,900,000	45 (25.7)	33 (19.2)	78 (22.5)	
2,000,000–2,900,000	39 (22.3)	57 (33.1)	96 (27.7)	
$\leq 1,900,000$	52 (29.7)	66 (38.4)	118 (34.0)	

Percentages are column percentages. p-values from Pearson's χ^2 test (sex: $\chi^2 = 1.528$, $df = 1$; education: $\chi^2 = 2.593$, $df = 3$; income: $\chi^2 = 16.476$, $df = 3$). CRC, colorectal cancer; IDR, Indonesian rupiah.

B. Validity and reliability of the questionnaire

All 23 exposure items showed positive item–total correlations ($r = 0.295$ – 0.737). Twenty-two items were significant at $p < 0.01$; the local processed food item (salted fish, instant noodles) showed a weaker correlation ($r = 0.295$, $p = 0.097$) but was retained as reported by the item analysis. Internal-consistency reliability of the 24-item instrument was high (Cronbach's $\alpha = 0.907$) (Table 3).

Table 3. Item validity (Pearson item–total correlation) and reliability of the food-frequency questionnaire

Domain	Item	Food item	r	p-value	Interpretation
X1 Red meat	X1.1	Beef satay	0.642	<0.001	Valid
	X1.2	Beef empal	0.658	<0.001	Valid
	X1.3	Beef rawon	0.701	<0.001	Valid
	X1.4	Beef krengsengan	0.711	<0.001	Valid
	X1.5	Beef tongseng	0.719	<0.001	Valid
	X1.6	Beef rendang	0.710	<0.001	Valid
	X1.7	Beef se'i	0.676	<0.001	Valid
	X1.8	Beef soto	0.698	<0.001	Valid
	X1.9	Goat satay	0.703	<0.001	Valid
	X1.10	Goat curry (gulai)	0.737	<0.001	Valid
	X1.11	Goat krengsengan	0.723	<0.001	Valid
	X1.12	Goat tengkleng	0.714	<0.001	Valid
	X1.13	Meatballs	0.491	0.003	Valid
	X1.14	Other meats (buffalo, pork, other four-legged animals)	0.565	<0.001	Valid
X2 Processed foods	X2.1	Western-style foods (pizza, breaded fried chicken, hot dog)	0.556	<0.001	Valid
	X2.2	Middle Eastern-style foods (kebab, roti maryam)	0.584	<0.001	Valid
	X2.3	Local processed foods (salted fish, instant noodles)	0.295	0.097	Retained†
	X2.4	Canned foods (sardines, tuna, canned gudeg)	0.533	<0.001	Valid
	X2.5	Sweet traditional processed foods (tape, layered cakes)	0.461	0.002	Valid
	X2.6	Wafers	0.552	<0.001	Valid
	X2.7	Biscuits	0.532	<0.001	Valid
	X2.8	Crackers	0.540	<0.001	Valid
	X2.9	Cookies	0.544	<0.001	Valid

Domain	Item	Food item	r	p-value	Interpretation
Reliability	—	Cronbach's α (24 items)	0.907	—	Reliable

†Classified as valid in the original item analysis; the correlation did not reach conventional significance and the item was retained for content reasons. r, Pearson correlation coefficient.

C. Normality testing

The Kolmogorov–Smirnov and Shapiro–Wilk tests yielded $p < 0.001$ for CRC status, the red meat items (X1.1–X1.14) and the processed food items (X2.1–X2.9), indicating non-normal distributions; non-parametric analyses were therefore applied (Supplementary Table S1 and Supplementary Figure S1).

D. Association between red meat consumption and colorectal cancer

Once-weekly red meat consumption was the most frequent category in both groups (53.7% of controls and 61.0% of cases), whereas consumption more than once weekly was reported by 13.7% of controls and 9.9% of cases (Table 4; Figure 3A). No cell had an expected count < 5 (minimum expected count 20.32). Pearson's χ^2 test showed no significant association between red meat consumption frequency and CRC ($\chi^2 = 2.235$, $df = 2$, $p = 0.327$), and there was no evidence of a linear trend (linear-by-linear association $p = 0.961$) (Table 5). Hypothesis H_1 was therefore rejected.

Table 4. Cross-tabulation of red meat consumption frequency by study group

Group	Statistic	<1 time/week	1 time/week	>1 time/week	Total
Controls	Count	57	94	24	175
	Expected count	54.0	100.4	20.7	175.0
	% within group	32.6%	53.7%	13.7%	100.0%
	% within frequency	53.3%	47.2%	58.5%	50.4%
CRC cases	Count	50	105	17	172
	Expected count	53.0	98.6	20.3	172.0
	% within group	29.1%	61.0%	9.9%	100.0%
	% within frequency	46.7%	52.8%	41.5%	49.6%
Total	Count	107	199	41	347
	% of total	30.8%	57.3%	11.8%	100.0%

Table 5. Chi-square tests for red meat consumption frequency and colorectal cancer

Test	Value	df	Asymptotic significance (two-sided)
Pearson χ^2	2.235	2	0.327
Likelihood ratio	2.242	2	0.326
Linear-by-linear association	0.002	1	0.961
N of valid cases	347		

0 cells (0.0%) had an expected count < 5 ; the minimum expected count was 20.32.

The Mann–Whitney U test likewise showed nearly identical rank distributions (mean rank 173.62 in controls vs. 174.38 in cases; $U = 14,984.0$; $Z = -0.080$; $p = 0.936$), indicating no difference in red meat consumption patterns between groups (Table 6).

Table 6. Mann–Whitney U test for red meat consumption frequency between controls and CRC cases

Group	n	Mean rank	Sum of ranks
Controls	175	173.62	30,384.0
CRC cases	172	174.38	29,994.0
Total	347		
Mann–Whitney U		14,984.0	
Z		−0.080	
Asymptotic significance (two-tailed)		0.936	

Grouping variable: CRC status. Mean ranks and rank sums were reconciled with the reported test statistics and verified against the cross-tabulated frequencies (Table 4).

E. Association between processed food consumption and colorectal cancer

Once-weekly processed food consumption was reported by 75.6% of cases compared with 62.3% of controls, whereas consumption <1 time/week was reported by 12.2% of cases and 22.9% of controls (Table 7; Figure 3B). Within the <1 time/week stratum, 65.6% of participants were controls, whereas within the once-weekly stratum 54.4% were cases. No cell had an expected count <5 (minimum expected count 23.30). Pearson's χ^2 test demonstrated a significant association between processed food consumption frequency and CRC ($\chi^2 = 8.270$, $df = 2$, $p = 0.016$; likelihood ratio $p = 0.015$), but the linear-by-linear association was not significant ($p = 0.181$) (Table 8). Hypothesis H_2 was therefore accepted.

Table 7. Cross-tabulation of processed food consumption frequency by study group

Group	Statistic	<1 time/week	1 time/week	>1 time/week	Total
Controls	Count	40	109	26	175
	Expected count	30.8	120.5	23.7	175.0
	% within group	22.9%	62.3%	14.9%	100.0%
	% within frequency	65.6%	45.6%	55.3%	50.4%
CRC cases	Count	21	130	21	172
	Expected count	30.2	118.5	23.3	172.0
	% within group	12.2%	75.6%	12.2%	100.0%
	% within frequency	34.4%	54.4%	44.7%	49.6%
Total	Count	61	239	47	347
	% of total	17.6%	68.9%	13.5%	100.0%

Table 8. Chi-square tests for processed food consumption frequency and colorectal cancer

Test	Value	df	Asymptotic significance (two-sided)
Pearson χ^2	8.270	2	0.016
Likelihood ratio	8.372	2	0.015
Linear-by-linear association	1.788	1	0.181
N of valid cases	347		

0 cells (0.0%) had an expected count <5; the minimum expected count was 23.30.

The Mann–Whitney U test showed a higher mean rank among cases (180.15) than among controls (167.96), consistent with more frequent processed food consumption in cases; however, the difference in the overall ordinal distribution did not reach statistical significance ($U = 13,993.0$; $Z = -1.387$; $p = 0.165$) (Table 9).

Table 9. Mann–Whitney U test for processed food consumption frequency between controls and CRC cases

Group	n	Mean rank	Sum of ranks
Controls	175	167.96	29,393.0
CRC cases	172	180.15	30,985.0
Total	347		
Mann–Whitney U		13,993.0	
Z		-1.387	
Asymptotic significance (two-tailed)		0.165	

Grouping variable: CRC status. Group assignment of mean ranks verified against the cross-tabulated frequencies (Table 7).

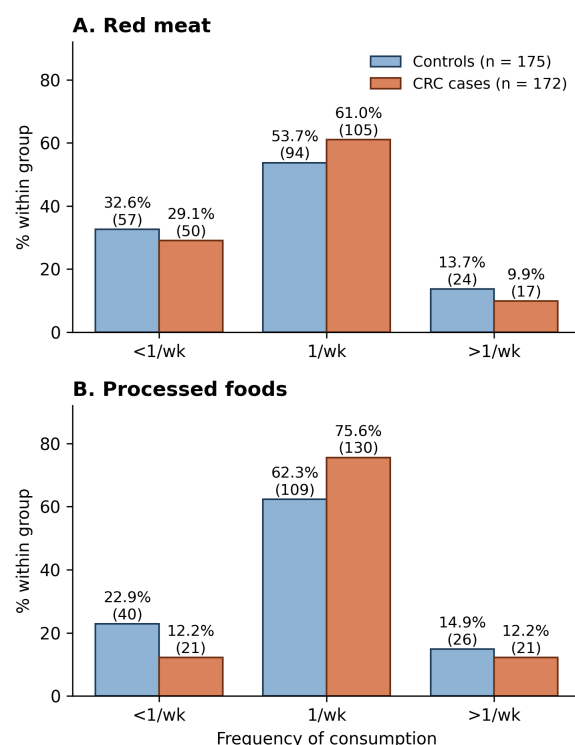


Figure 3. Distribution of consumption frequency among controls and colorectal cancer cases. (A) Red meat; (B) processed foods. Values are percentages within each study group, with absolute counts in parentheses.

F. Odds ratios for consumption frequency

Compared with red meat consumption <1 time/week, the crude OR for CRC was 1.27 (95% CI 0.80–2.04; $p = 0.314$) for once-weekly consumption and 0.81 (95% CI 0.39–1.67; $p = 0.565$) for consumption more than once weekly; all CIs crossed unity (Table 10). For processed foods, once-weekly consumption was associated with 2.27-fold higher odds of CRC (95% CI 1.26–4.08; $p = 0.006$) relative to <1 time/week, with a lower confidence limit above unity. Consumption more than once weekly yielded an OR of 1.54 (95% CI 0.70–3.36; $p = 0.280$), which was not significant. When both higher-frequency categories were combined, any processed food consumption ≥ 1 time/week remained associated with CRC (OR 2.13; 95% CI 1.20–3.79; $p = 0.010$), whereas the corresponding estimate for red meat was null (OR 1.18; 95% CI 0.75–1.86; $p = 0.480$) (Table 11; Figure 4).

Table 10. Crude odds ratios for the association between red meat consumption frequency and colorectal cancer

Consumption frequency	CRC cases (n)	Controls (n)	Crude OR	95% CI	p-value
<1 time/week	50	57	1.00	Reference	—
1 time/week	105	94	1.27	0.80–2.04	0.314
>1 time/week	17	24	0.81	0.39–1.67	0.565
≥ 1 time/week (any)*	122	118	1.18	0.75–1.86	0.480

OR, odds ratio; CI, confidence interval (Woolf method); p-values from the Wald test. *Supplementary pooled contrast (1 and >1 time/week combined vs. <1 time/week).

Table 11. Crude odds ratios for the association between processed food consumption frequency and colorectal cancer

Consumption frequency	CRC cases (n)	Controls (n)	Crude OR	95% CI	p-value
<1 time/week	21	40	1.00	Reference	—
1 time/week	130	109	2.27	1.26–4.08	0.006
>1 time/week	21	26	1.54	0.70–3.36	0.280
≥ 1 time/week (any)*	151	135	2.13	1.20–3.79	0.010

OR, odds ratio; CI, confidence interval (Woolf method); p-values from the Wald test. *Supplementary pooled contrast (1 and >1 time/week combined vs. <1 time/week).

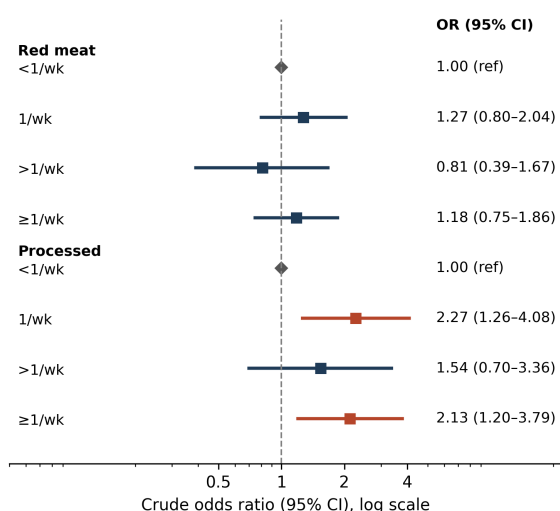


Figure 4. Forest plot of crude odds ratios (95% confidence intervals) for colorectal cancer according to consumption frequency, with <1 time/week as reference. Red markers indicate estimates whose confidence interval excludes unity.

IV. DISCUSSION

A. Principal findings

In this multicentre case–control study of 347 adults in East Java, the frequency of red meat consumption was not associated with CRC, whereas processed food consumption was significantly associated with CRC, with once-weekly consumption conferring 2.27-fold higher crude odds than consumption less than once weekly. The association did not follow a monotonic dose–response gradient, as the highest-frequency category (>1 time/week) yielded an attenuated and non-significant estimate. These findings are broadly consistent with the international consensus that processed meat is the more robust dietary carcinogen, while illustrating the heterogeneity of the red meat–CRC relationship in Asian populations.^{22,23,33}

B. Participant characteristics

The sex distribution was balanced, and although men were slightly over-represented among cases, the difference was not significant. International data consistently show a higher CRC risk in men, a pattern attributed to hormonal influences, genetic susceptibility and a higher prevalence of adverse lifestyle behaviours such as frequent meat intake, smoking and alcohol consumption. In an Indonesian hospital-based study at Dr. Pirngadi Regional General Hospital, Medan, both age and male sex were significantly associated with CRC occurrence.^{1,3,44}

Educational attainment did not differ significantly between groups, although junior-high-school education was somewhat more common among cases. By contrast, income differed markedly, with cases concentrated in the lowest income strata. Socioeconomic position is closely linked to dietary quality, access to health information and screening, and health-seeking behaviour; in East Java, cultural values and self-health awareness have been identified as important predictors of health-seeking behaviour among CRC patients. Because income may relate both to dietary patterns (including reliance on inexpensive processed foods) and to CRC diagnosis, it represents a potential confounder that could not be adjusted for in the present crude analysis.^{12,38,45}

C. Red meat consumption and colorectal cancer

The absence of an association between red meat frequency and CRC contrasts with several large prospective cohorts and meta-analyses, including EPIC and pooled analyses reporting 14–22% increases in risk with high intake, and with IARC's classification of red meat as probably carcinogenic. However, our finding is concordant with a meta-analysis of East-Asian observational studies from China, Japan and South Korea that found no

significant association (pooled OR 1.38; 95% CI 0.98–1.93) and with an Asian-perspective review noting that most studies conducted in Asia do not support a clear association. Moreover, in patients with stage III colon cancer, red meat intake was not associated with recurrence or mortality.^{24,26,28,29,32,33,46}

Several explanations are plausible. First, cumulative exposure in this population may be relatively low: more than 88% of participants consumed red meat once weekly or less, well below the intakes (e.g., >50–100 g/day or more than once daily) at which risk increments were observed in Western studies. Second, the exposure metric captured frequency but not portion size, cumulative lifetime intake or doneness, all of which influence the formation of heterocyclic amines and polycyclic aromatic hydrocarbons. Third, local preparations such as rawon, soto and gulai are predominantly boiled or simmered, whereas grilling (as in satay) represents a smaller share of intake; cooking temperature strongly modulates carcinogen formation.^{26,27,47,48}

Population heterogeneity may also have contributed. East Java comprises culturally distinct groups with diverse socioeconomic conditions, lifestyles and access to health services. Genetic susceptibility further modifies the effect of meat-derived carcinogens: polymorphisms in metabolic genes such as CYP2E1 and PPAR γ and genome-wide gene–environment interactions have been shown to modify the association between red or processed meat intake and CRC, and host genetic variants shape tumour biology and treatment response. Finally, the modest sample size limited the power to detect small effects of the magnitude reported in meta-analyses (relative risks of approximately 1.1–1.2).^{12,28,49–51}

D. Processed food consumption and colorectal cancer

The significant association between processed food consumption and CRC in East Java aligns with the IARC Group 1 classification of processed meat and with meta-analyses reporting an approximately 18% higher CRC risk per 50 g/day of processed meat. Processing techniques such as curing, smoking and the addition of nitrates or nitrites promote the formation of N-nitroso compounds and polycyclic aromatic hydrocarbons, and nitrosyl-haem in processed meat enhances endogenous N-nitrosation.^{22,26,28,52,53}

Notably, the processed food exposure in this study extended beyond processed meat to include Western-style fast foods, Middle Eastern-style foods, locally preserved foods such as salted fish and instant noodles, canned foods and processed snacks, many of which fall within the ultra-processed food category. Meta-analyses and large prospective cohorts have associated higher ultra-processed food intake with increased CRC risk—particularly among men—through mechanisms including nutrient displacement, obesity-related pathways, food additives and neo-formed contaminants. Our findings therefore extend evidence on processed and ultra-processed foods to an Indonesian setting where such products are increasingly consumed.^{54–56}

The lack of a monotonic dose–response gradient warrants cautious interpretation. The >1 time/week category contained only 47 participants, producing wide confidence intervals and unstable estimates; in addition, the three-level frequency scale may have compressed heterogeneous intakes into a single category. Reverse causation is also possible, as patients with advanced CRC may have reduced their intake of certain foods because of gastrointestinal symptoms, and differential recall between cases and controls may have biased the upper category. Similar absence of a dose–response relationship has been reported in meta-analyses of ultra-processed foods despite significant high-versus-low associations.^{54,56}

E. Biological plausibility

Several mechanisms support a causal role of red and processed meat in colorectal carcinogenesis. Haem iron catalyses endogenous formation of N-nitroso compounds and lipid

peroxidation, producing cytotoxic and genotoxic aldehydes; experimental studies show that dietary haem induces oxidative stress, cytotoxicity and compensatory epithelial hyperproliferation, and that Apc-mutated colonocytes resist haem-induced lipoperoxide apoptosis, conferring a selective advantage to premalignant cells. A meta-analysis of prospective cohorts reported a relative risk of 1.18 for colon cancer in the highest category of haem intake.^{57–60}

Additional pathways include heterocyclic amines such as MeIQx and DiMeIQx formed during high-temperature cooking, secondary bile acid production and dysbiosis promoted by high-fat red meat, and metabolic incorporation of the non-human sialic acid N-glycolylneuraminic acid (Neu5Gc), which may trigger chronic xenosialitis. Changes in the nutrient composition of meat, including its fat content, may further influence these pathways. These mechanisms converge on DNA damage, inflammation and Wnt pathway activation, consistent with the molecular pathogenesis of CRC.^{14,16,31,47,61,62}

F. Other contributing factors

CRC is a multifactorial disease. Smoking, physical inactivity, alcohol consumption, obesity, low fibre intake and family history are established contributors, and adherence to multiple healthy lifestyle factors is associated with substantially lower CRC risk in a dose-dependent manner. Dietary and nutritional status also influence outcomes in patients with established CRC. The unmeasured distribution of these factors in the present sample may have confounded or modified the observed associations.^{7,18,35,45}

G. Comparison with previous studies

Our results mirror the pattern described in reports from WCRF/AICR and in meta-analyses of prospective studies, in which processed meat shows a more consistent association with CRC than unprocessed red meat. Conversely, the red meat findings are more closely aligned with Asian than Western evidence: a 2025 meta-analysis of Asian case–control studies reported a significant pooled association for red meat but not for processed meat, while an East-Asian meta-analysis found no significant association for red meat, emphasising heterogeneity by region, study design and exposure definition. Differences in meat subtypes further contribute, as beef, pork, lamb and processed products appear to carry different magnitudes of risk.^{23,25,26,30,32,34}

H. Strengths and limitations

The strengths of this study include its multicentre recruitment across several East Java regencies, histopathological confirmation of all cases, and the use of a culturally adapted FFQ with local dishes and a broad processed food spectrum that demonstrated excellent internal consistency ($\alpha = 0.907$).^{12,41}

Several limitations should be acknowledged. First, the retrospective case–control design precludes causal inference and is vulnerable to recall and selection bias; controls were not individually matched and the control source was not formally characterised. Second, exposure was assessed by frequency only, without portion size, cumulative duration, cooking method or energy adjustment, which may have led to non-differential misclassification biasing estimates towards the null. Third, the ORs were crude and were not adjusted for age, sex, income, body mass index, smoking, alcohol, physical activity, fibre intake or family history through multivariable logistic regression; the significant income imbalance is particularly relevant. Fourth, the upper exposure categories contained few participants, resulting in imprecise estimates. Fifth, one processed food item showed weak item–total correlation during pilot validation. Finally, as data were collected in referral centres and a stoma community within a single province, generalisability to other Indonesian populations may be limited.^{36,37,54}

I. Implications

Despite these limitations, the findings support current recommendations to limit processed food consumption as part of CRC prevention and provide a basis for context-specific public-health interventions in East Java, including community nutrition education, clearer health-risk labelling of processed products, and integration of CRC risk counselling and screening into routine services at regional hospitals and community health centres (Puskesmas). From a clinical perspective, surgeons and primary-care physicians should incorporate dietary counselling—limiting processed foods and encouraging fibre-rich plant foods—into CRC prevention and survivorship care.^{23,35,38,39}

V. CONCLUSION AND RECOMMENDATIONS

A. Conclusion

In this multicentre case–control study in East Java, the frequency of red meat consumption was not significantly associated with CRC, and no dose–response relationship was observed. Processed food consumption was significantly associated with CRC, with once-weekly consumption conferring approximately 2.3-fold higher crude odds, although the association was not consistent across higher consumption frequencies. Processed food consumption may therefore represent a relevant modifiable dietary risk factor for CRC in this population, but the findings should be interpreted with caution given the crude nature of the estimates and the absence of adjustment for key confounders.^{22,23}

B. Recommendations

For the community. Limit the consumption of processed foods and processed meats containing nitrates or nitrites, adopt a balanced diet rich in vegetables, fruits and dietary fibre, and reduce intake of foods high in fat and preservatives.^{23,45}

For healthcare professionals. Provide education on healthy dietary habits that emphasises limiting processed food intake alongside moderation of red meat, deliver nutritional and lifestyle counselling, and actively implement CRC screening for individuals at increased risk.^{38,39}

For future research. Employ prospective cohort or matched case–control designs with multivariable logistic regression; assess portion size, cumulative intake, food type, and cooking and processing methods; and measure physical activity, body mass index, smoking, alcohol, family history and fibre intake to enable adjustment and effect-modification analyses.^{28,50}

For healthcare institutions and policymakers. Develop CRC prevention programmes focused on healthy diets, strengthen regulation and monitoring of food additives in processed products, mandate clear nutritional and health-risk labelling, and encourage the food industry to develop products with lower concentrations of potentially carcinogenic compounds.^{22,52}

VI. DECLARATIONS

Acknowledgements: The authors thank the Head of the Surgical Specialist Education Programme, Faculty of Medicine, Universitas Brawijaya, the members of the examining committee, and all staff and participants at the participating centres.

Author contributions: TH: conceptualisation, data collection, formal analysis, writing—original draft. AB: supervision, methodology, writing—review and editing. AE: statistical methodology and formal analysis, writing—review and editing. All authors approved the final manuscript.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflicts of interest: The authors declare no conflicts of interest.

Ethics approval: Approved by the Health Research Ethics Committee [name and approval number to be inserted].

Data availability: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

VII. REFERENCES

- [1]. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021;71(3):209–49. doi:10.3322/caac.21660. Available from: <https://doi.org/10.3322/caac.21660>
- [2]. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394–424. doi:10.3322/caac.21492. Available from: <https://doi.org/10.3322/caac.21492>
- [3]. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer.* 2010;127(12):2893–917. doi:10.1002/ijc.25516. Available from: <https://doi.org/10.1002/ijc.25516>
- [4]. Dekker E, Tanis PJ, Vleugels JLA, Kasi PM, Wallace MB. Colorectal cancer. *Lancet.* 2019;394(10207):1467–80. doi:10.1016/S0140-6736(19)32319-0. Available from: [https://doi.org/10.1016/S0140-6736\(19\)32319-0](https://doi.org/10.1016/S0140-6736(19)32319-0)
- [5]. Kuipers EJ, Grady WM, Lieberman D, Seufferlein T, Sung JJ, Boelens PG, et al. Colorectal cancer. *Nat Rev Dis Primers.* 2015;1:15065. doi:10.1038/nrdp.2015.65. Available from: <https://doi.org/10.1038/nrdp.2015.65>
- [6]. Baidoun F, Elshawy K, Elkeriaie Y, Merjaneh Z, Khoudari G, Sarmini MT, et al. Colorectal cancer epidemiology: recent trends and impact on outcomes. *Curr Drug Targets.* 2021;22(9):998–1009. doi:10.2174/138945012199920111715717. Available from: <https://doi.org/10.2174/138945012199920111715717>
- [7]. Patel SG, Karlitz JJ, Yen T, Lieu CH, Boland CR. The rising tide of early-onset colorectal cancer: a comprehensive review of epidemiology, clinical features, biology, risk factors, prevention, and early detection. *Lancet Gastroenterol Hepatol.* 2022;7(3):262–74. doi:10.1016/S2468-1253(21)00426-X. Available from: [https://doi.org/10.1016/S2468-1253\(21\)00426-X](https://doi.org/10.1016/S2468-1253(21)00426-X)
- [8]. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol.* 2022;20(6):1229–40.e5. doi:10.1016/j.cgh.2021.01.037. Available from: <https://doi.org/10.1016/j.cgh.2021.01.037>
- [9]. Loomans-Kropp HA, Umar A. Increasing incidence of colorectal cancer in young adults. *J Cancer Epidemiol.* 2019;2019:9841295. doi:10.1155/2019/9841295. Available from: <https://doi.org/10.1155/2019/9841295>
- [10]. Danpanichkul P, Moolkaew P, Kanjanakot Y, Polpichai N, Jaroenlapnopparat A, Kim D, et al. Rising incidence and impact of early-onset colorectal cancer in the Asia-Pacific with higher mortality in females from Southeast Asia: a global burden analysis from 2010 to 2019. *J Gastroenterol Hepatol.* 2023;38(12):2053–60. doi:10.1111/jgh.16331. Available from: <https://doi.org/10.1111/jgh.16331>
- [11]. Widhyasih RM, Rahmadhanti SD, Fajrunni'mah R. Carcinoembryonic antigen (CEA) dan neutrofil-to-limfosit ratio (NLR) sebagai faktor prediktif kanker kolorektal. *J Ilmu Teknol Kesehat.* 2019;7(1):68–76. doi:10.32668/jitek.v7i1.223. Available from: <https://doi.org/10.32668/jitek.v7i1.223>
- [12]. Budianto A, Andarini S, Hariyanti T, Muslihah N. The relationship between ethnicity and health seeking behavior for colorectal cancer in East Java, Indonesia: a case study of Arek, Mataraman, and Pendulangan ethnic groups. *Asian Pac J Cancer Prev.* 2023;24(6):1931–42. doi:10.31557/APJCP.2023.24.6.1931. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10505871>
- [13]. Sullivan BA, Noujaim M, Roper J. Cause, epidemiology, and histology of polyps and pathways to colorectal cancer. *Gastrointest Endosc Clin N Am.* 2022;32(2):177–94. doi:10.1016/j.giec.2021.12.001. Available from: <https://doi.org/10.1016/j.giec.2021.12.001>
- [14]. Zhao H, Ming T, Tang S, Ren S, Yang H, Liu M, et al. Wnt signaling in colorectal cancer: pathogenic role and therapeutic target. *Mol Cancer.* 2022;21(1):144. doi:10.1186/s12943-022-01616-7. Available from: <https://doi.org/10.1186/s12943-022-01616-7>
- [15]. Copija A, Waniczek D, Witkoś A, Walkiewicz K, Nowakowska-Zajdel E. Clinical significance and prognostic relevance of microsatellite instability in sporadic colorectal cancer patients. *Int J Mol Sci.* 2017;18(1):107. doi:10.3390/ijms18010107. Available from: <https://doi.org/10.3390/ijms18010107>
- [16]. Schmitt M, Greten FR. The inflammatory pathogenesis of colorectal cancer. *Nat Rev Immunol.* 2021;21(10):653–67. doi:10.1038/s41577-021-00534-x. Available from: <https://doi.org/10.1038/s41577-021-00534-x>
- [17]. Sawicki T, Ruszkowska M, Danielewicz A, Niedzwiedzka E, Arlukowicz T, Przybyłowicz KE. A review of colorectal cancer in terms of epidemiology, risk factors, development, symptoms and diagnosis. *Cancers (Basel).* 2021;13(9):2025. doi:10.3390/cancers13092025. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC8122718>
- [18]. Sninsky JA, Shore BM, Lupu GV, Crockett SD. Risk factors for colorectal polyps and cancer. *Gastrointest Endosc Clin N Am.* 2022;32(2):195–213. doi:10.1016/j.giec.2021.12.008. Available from: <https://doi.org/10.1016/j.giec.2021.12.008>
- [19]. Ionescu VA, Gheorghe G, Bacalbasa N, Chiotoroiu AL, Diaconu C. Colorectal cancer: from risk factors to oncogenesis. *Medicina (Kaunas).* 2023;59(9):1646. doi:10.3390/medicina59091646. Available from: <https://doi.org/10.3390/medicina59091646>
- [20]. Song X, Gong X, Zhang T, Jiang W. Height and risk of colorectal cancer: a meta-analysis. *Eur J Cancer Prev.* 2018;27(6):521–9. doi:10.1097/CEJ.0000000000000390. Available from: <https://doi.org/10.1097/CEJ.0000000000000390>
- [21]. Hur SJ, Yoon Y, Jo C, Jeong JY, Lee KT. Effect of dietary red meat on colorectal cancer risk—a review. *Compr Rev Food Sci Food Saf.* 2019;18(6):1812–24. doi:10.1111/1541-4337.12501. Available from: <https://doi.org/10.1111/1541-4337.12501>
- [22]. Bouvard V, Loomis D, Guyton KZ, Grosse Y, El Ghissassi F, Benbrahim-Tallaa L, et al. Carcinogenicity of consumption of red and processed meat. *Lancet Oncol.* 2015;16(16):1599–600. doi:10.1016/S1470-2045(15)00444-1. Available from: [https://doi.org/10.1016/S1470-2045\(15\)00444-1](https://doi.org/10.1016/S1470-2045(15)00444-1)
- [23]. World Cancer Research Fund/American Institute for Cancer Research. Diet, nutrition, physical activity and colorectal cancer. Continuous Update Project Expert Report 2018. London: WCRF International; 2018. Available from: <https://www.wcrf.org/>
- [24]. Aykan NF. Red meat and colorectal cancer. *Oncol Rev.* 2015;9(1):288. doi:10.4081/oncol.2015.288. Available from: <https://doi.org/10.4081/oncol.2015.288>
- [25]. Carr PR, Walter V, Brenner H, Hoffmeister M. Meat subtypes and their association with colorectal cancer: systematic review and meta-analysis. *Int J Cancer.* 2016;138(2):293–302. doi:10.1002/ijc.29423. Available from: <https://doi.org/10.1002/ijc.29423>
- [26]. Chan DSM, Lau R, Aune D, Vieira R, Greenwood DC, Kampman E, et al. Red and processed meat and colorectal cancer incidence: meta-analysis of prospective studies. *PLoS One.* 2011;6(6):e20456. doi:10.1371/journal.pone.0020456. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC3108955>
- [27]. Smolińska K, Paluszkievicz P. Risk of colorectal cancer in relation to frequency and total amount of red meat consumption. Systematic review and meta-analysis. *Arch Med Sci.* 2010;6(4):605–10. Available from: https://www.termedia.pl/Journal/Archives_of_Medical_Science-19/Streszczenie-15186
- [28]. Farvid MS, Sidahmed E, Spence ND, et al. Consumption of red meat and processed meat and cancer incidence: a systematic review and meta-analysis of prospective studies. *Eur J Epidemiol.* 2021;36(9):937–51. doi:10.1007/s10654-021-00741-9. Available from: <https://doi.org/10.1007/s10654-021-00741-9>
- [29]. Ungvari Z, Fekete M, Varga P, Lehoczi A, Munkácsy G, Fekete JT, et al. Association between red and processed meat consumption and colorectal cancer risk: a comprehensive meta-analysis of prospective studies. *GeroScience.* 2025;47(3):5123–40. doi:10.1007/s11357-025-01646-1. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC12181564>
- [30]. Zhao Z, Feng Q, Yin Z, Shuang J, Bai B, Yu P, et al. Red and processed meat consumption and colorectal cancer risk: a systematic review and meta-analysis. *Oncotarget.* 2017;8(47):83306–14. doi:10.18632/oncotarget.20667. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC5669970>
- [31]. Diakité MT, Diakité B, Koné A, Balam S, Fofana D, Diallo D, et al. Relationships between gut microbiota, red meat consumption and colorectal cancer. *J Carcinog Mutagen.* 2022;13. Available from: <https://consensus.app/papers/details/e723b57ae81850ec939994e7be5e2320/>
- [32]. Cheung HS, Lu LY, So WL, Wong HW, Wong SH, Mak CM. Association of red meat intake and colorectal cancer among East-Asians: a systematic review and meta-analysis of observational studies performed between 2011–2021. *J Gastrointest Liver Dis.* 2023;32(3):377–83. doi:10.15403/jgld-4778. Available from: <https://doi.org/10.15403/jgld-4778>
- [33]. Hur SJ, Jo C, Yoon Y, Jeong JY, Lee KT. Controversy on the correlation of red and processed meat consumption with colorectal cancer risk: an Asian perspective. *Crit Rev Food Sci Nutr.* 2019;59(21):3526–37. doi:10.1080/10408398.2018.1495615. Available from: <https://doi.org/10.1080/10408398.2018.1495615>
- [34]. Liao Z, Wu W, Xia S, Yu L, Xu Z, Li Y. Associations between the consumption of red meat and processed meat and the incidence of colorectal cancer in Asia: a meta-analysis. *Front Med (Lausanne).* 2025;12:1555717. doi:10.3389/fmed.2025.1555717. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC12183693>
- [35]. Minhaj R, Harjianti T, Rasyid H, Bukhari A, Islam IC, Zainal ATF, et al. Colorectal cancer patients' outcome in correlation with dietary and nutritional status: a systematic review. *Ann Med.* 2023;55(2):2281662. doi:10.1080/07853890.2023.2281662. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10986434>
- [36]. Masturoh I, Anggita T N. Metodologi penelitian kesehatan. Bahan Ajar Rekam Medis dan Informasi Kesehatan. Jakarta: Kementerian Kesehatan Republik Indonesia; 2018.
- [37]. Sumantri A. Metodologi penelitian kesehatan. Jakarta: Prenada Media; 2015.
- [38]. Kanth P, Inadomi JM. Screening and prevention of colorectal cancer. *BMJ.* 2021;374:n1855. doi:10.1136/bmj.n1855. Available from: <https://doi.org/10.1136/bmj.n1855>
- [39]. US Preventive Services Task Force; Davidson KW, Barry MJ, Mangione CM, Cabana M, Caughey AB, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. *JAMA.* 2021;325(19):1965–77. doi:10.1001/jama.2021.6238. Available from: <https://doi.org/10.1001/jama.2021.6238>

- [40]. Papalampros AE, Petrou AS, Mantonakis EI, Evangelou KI, Giannopoulos LA, Marinos GG, et al. Coexistence of a colon carcinoma with two distinct renal cell carcinomas: a case report. *J Med Case Rep*. 2011;5:134. doi:10.1186/1752-1947-5-134. Available from: <https://doi.org/10.1186/1752-1947-5-134>
- [41]. Swarjana IK. Metodologi penelitian kesehatan. Yogyakarta: Penerbit Andi; 2012.
- [42]. Yoshino T, Argilés G, Oki E, Martinelli E, Taniguchi H, Arnold D, et al. Pan-Asian adapted ESMO Clinical Practice Guidelines for the diagnosis, treatment and follow-up of patients with localised colon cancer. *Ann Oncol*. 2021;32(12):1496–510. doi:10.1016/j.annonc.2021.08.1752. Available from: <https://doi.org/10.1016/j.annonc.2021.08.1752>
- [43]. Biller LH, Schrag D. Diagnosis and treatment of metastatic colorectal cancer: a review. *JAMA*. 2021;325(7):669–85. doi:10.1001/jama.2021.0106. Available from: <https://doi.org/10.1001/jama.2021.0106>
- [44]. Adila A, Mustika SE. Hubungan usia dan jenis kelamin terhadap kejadian kanker kolorektal. *J Kedokt STM (Sains Teknol Med)*. 2023;6(1):53–9. doi:10.30743/stm.v6i1.349. Available from: <https://doi.org/10.30743/stm.v6i1.349>
- [45]. Yu J, Feng Q, Kim JH, Zhu Y. Combined effect of healthy lifestyle factors and risks of colorectal adenoma, colorectal cancer, and colorectal cancer mortality: systematic review and meta-analysis. *Front Oncol*. 2022;12:827019. doi:10.3389/fonc.2022.827019. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9353059>
- [46]. Van Blarigan EL, Ou FS, Bainter TM, Fuchs CS, Niedzwiecki D, Zhang S, et al. Associations between unprocessed red meat and processed meat with risk of recurrence and mortality in patients with stage III colon cancer. *JAMA Netw Open*. 2022;5(2):e220145. doi:10.1001/jamanetworkopen.2022.0145. Available from: <https://doi.org/10.1001/jamanetworkopen.2022.0145>
- [47]. Cross AJ, Ferrucci LM, Risch A, Graubard BI, Ward MH, Park Y, et al. A large prospective study of meat consumption and colorectal cancer risk: an investigation of potential mechanisms underlying this association. *Cancer Res*. 2010;70(6):2406–14. doi:10.1158/0008-5472.CAN-09-3929. Available from: <https://doi.org/10.1158/0008-5472.CAN-09-3929>
- [48]. Kossenas K, Constantinou C. Epidemiology, molecular mechanisms, and clinical trials: an update on research on the association between red meat consumption and colorectal cancer. *Curr Nutr Rep*. 2021;10(4). doi:10.1007/s13668-021-00377-x. Available from: <https://doi.org/10.1007/s13668-021-00377-x>
- [49]. Kim NH, Seol JE, Kim J, Lee BH, Hwang DY, Jeong J, et al. Red meat intake, CYP2E1 and PPAR γ polymorphisms, and colorectal cancer risk. *Eur J Cancer Prev*. 2019;28(4):304–10. doi:10.1097/CEJ.0000000000000462. Available from: <https://doi.org/10.1097/CEJ.0000000000000462>
- [50]. Stern MC, Sanchez Mendez J, Kim AE, Obón-Santacana M, Moratalla-Navarro F, Martín V, et al. Genome-wide gene–environment interaction analyses to understand the relationship between red meat and processed meat intake and colorectal cancer risk. *Cancer Epidemiol Biomarkers Prev*. 2024;33(3):400–10. doi:10.1158/1055-9965.EPI-23-0717. Available from: <https://doi.org/10.1158/1055-9965.EPI-23-0717>
- [51]. Bahrami A, Amerizadeh F, Hassanian SM, ShahidSales S, Khazaei M, Maftouh M, et al. Genetic variants as potential predictive biomarkers in advanced colorectal cancer patients treated with oxaliplatin-based chemotherapy. *J Cell Physiol*. 2018;233(3):2193–201. doi:10.1002/jcp.25966. Available from: <https://doi.org/10.1002/jcp.25966>
- [52]. Demeyer D, Mertens B, De Smet S, Ulens M. Mechanisms linking colorectal cancer to the consumption of (processed) red meat: a review. *Crit Rev Food Sci Nutr*. 2016;56(16):2747–66. doi:10.1080/10408398.2013.873886. Available from: <https://doi.org/10.1080/10408398.2013.873886>
- [53]. Cross AJ, Pollock JRA, Bingham SA. Haem, not protein or inorganic iron, is responsible for endogenous intestinal N-nitrosation arising from red meat. *Cancer Res*. 2003;63(10):2358–60. PMID: 12750250. Available from: <https://pubmed.ncbi.nlm.nih.gov/12750250>
- [54]. Isaksen IM, Dankel SN. Ultra-processed food consumption and cancer risk: a systematic review and meta-analysis. *Clin Nutr*. 2023;42(6):919–28. doi:10.1016/j.clnu.2023.03.018. Available from: <https://doi.org/10.1016/j.clnu.2023.03.018>
- [55]. Wang L, Du M, Wang K, Khandpur N, Rossato SL, Drouin-Chartier JP, et al. Association of ultra-processed food consumption with colorectal cancer risk among men and women: results from three prospective US cohort studies. *BMJ*. 2022;378:e068921. doi:10.1136/bmj-2021-068921. Available from: <https://doi.org/10.1136/bmj-2021-068921>
- [56]. Shu L, Huang Y, Si C, Zhu Q, Zheng P, Zhang X. Association between ultra-processed food intake and risk of colorectal cancer: a systematic review and meta-analysis. *Front Nutr*. 2023;10:1170992. doi:10.3389/fnut.2023.1170992. Available from: <https://doi.org/10.3389/fnut.2023.1170992>
- [57]. Bastide NM, Pierre FHF, Corpet DE. Heme iron from meat and risk of colorectal cancer: a meta-analysis and a review of the mechanisms involved. *Cancer Prev Res (Phila)*. 2011;4(2):177–84. doi:10.1158/1940-6207.CAPR-10-0113. Available from: <https://doi.org/10.1158/1940-6207.CAPR-10-0113>
- [58]. IJssennaggar N, Rijnierse A, de Wit NJ, Boekschoten MV, Dekker J, Schonewille A, et al. Dietary heme induces acute oxidative stress, but delayed cytotoxicity and compensatory hyperproliferation in mouse colon. *Carcinogenesis*. 2013;34(7):1628–35. doi:10.1093/carcin/bgt084. Available from: <https://doi.org/10.1093/carcin/bgt084>
- [59]. Pierre F, Taché S, Petit CR, et al. Apc mutation induces resistance of colonic cells to lipoperoxide-triggered apoptosis induced by faecal water from haem-fed rats. *Carcinogenesis*. 2007;28(2):321–7. doi:10.1093/carcin/bgl127. Available from: <https://doi.org/10.1093/carcin/bgl127>
- [60]. Turner ND, Lloyd SK. Association between red meat consumption and colon cancer: a systematic review of experimental results. *Exp Biol Med (Maywood)*. 2017;242(8):813–39. doi:10.1177/1535370217693117. Available from: <https://doi.org/10.1177/1535370217693117>
- [61]. Alisson-Silva F, Kawanishi K, Varki A. Human risk of diseases associated with red meat intake: analysis of current theories and proposed role for metabolic incorporation of a non-human sialic acid. *Mol Aspects Med*. 2016;51:16–30. doi:10.1016/j.mam.2016.07.002. Available from: <https://doi.org/10.1016/j.mam.2016.07.002>
- [62]. Schönfeldt HC, Gibson N. Changes in the nutrient quality of meat in an obesity context. *Meat Sci*. 2008;80(1):20–7. doi:10.1016/j.meatsci.2008.05.025. Available from: <https://doi.org/10.1016/j.meatsci.2008.05.025>

SUPPLEMENTARY MATERIAL

Supplementary Table S1. Tests of normality for colorectal cancer status and questionnaire items (n = 347)

Variable	Kolmogorov–Smirnov statistic	df	p	Shapiro–Wilk statistic	df	p
CRC status	0.343	347	<0.001	0.636	347	<0.001
X1.1	0.502	347	<0.001	0.437	347	<0.001
X1.2	0.460	347	<0.001	0.554	347	<0.001
X1.3	0.456	347	<0.001	0.563	347	<0.001
X1.4	0.500	347	<0.001	0.442	347	<0.001
X1.5	0.512	347	<0.001	0.402	347	<0.001
X1.6	0.486	347	<0.001	0.489	347	<0.001
X1.7	0.532	347	<0.001	0.285	347	<0.001
X1.8	0.474	347	<0.001	0.522	347	<0.001
X1.9	0.506	347	<0.001	0.423	347	<0.001
X1.10	0.516	347	<0.001	0.387	347	<0.001
X1.11	0.522	347	<0.001	0.354	347	<0.001
X1.12	0.532	347	<0.001	0.293	347	<0.001
X1.13	0.310	347	<0.001	0.752	347	<0.001
X1.14	0.535	347	<0.001	0.257	347	<0.001
X2.1	0.511	347	<0.001	0.408	347	<0.001
X2.2	0.530	347	<0.001	0.292	347	<0.001
X2.3	0.262	347	<0.001	0.766	347	<0.001
X2.4	0.510	347	<0.001	0.412	347	<0.001
X2.5	0.343	347	<0.001	0.723	347	<0.001
X2.6	0.399	347	<0.001	0.658	347	<0.001
X2.7	0.364	347	<0.001	0.697	347	<0.001
X2.8	0.449	347	<0.001	0.577	347	<0.001
X2.9	0.453	347	<0.001	0.569	347	<0.001

Lilliefors significance correction applied to the Kolmogorov–Smirnov test.