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Original Research Article

Dietary-Lifestyle Patterns and Colorectal Cancer Risk: Global Cancer Update Programme (CUP Global) Systematic Literature Review

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ABSTRACT

Background: Although healthy dietary and lifestyle factors have been individually linked to lower colorectal cancer (CRC) risks, recommendations for whole diet-lifestyle patterns remained unestablished because of limited studies and inconsistent pattern definitions.

Objectives: This updated review synthesized literature on dietary-lifestyle patterns and CRC risk/mortality.

Methods: PubMed and Embase were searched through March 31, 2023 for randomized controlled trials and prospective cohort studies examining adulthood dietary patterns combined with modifiable lifestyle factors such as adiposity, smoking, alcohol consumption, physical activity, and/or others. Patterns were categorized by derivation methods: a priori, a posteriori, and a hybrid combining both; and were then descriptively reviewed for the primary outcomes: CRC risk or mortality. The Global Cancer Update Programme Expert Committee and Expert Panel independently graded the evidence on the likelihood of causality using predefined grading criteria.

Results: Thirty-three observational studies were reviewed. "Strong-probable" evidence was concluded for higher levels of alignment with the a priori-derived World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) recommendations score and lower CRC risk; and "limited-suggestive" evidence for the American Cancer Society guidelines and Healthy Lifestyle Index with lower CRC risk (mainly because of concerns about risk of bias for confounding). A posteriori-derived patterns lack firm evidence (only 1 study). "Strong-probable" evidence was concluded for higher levels of alignment with the Empirical Lifestyle Index for Hyperinsulinemia hybrid pattern and higher CRC risk. By cancer subsite, only the WCRF/AICR recommendations score showed "strong-probable" evidence with lower colon cancer risk. All exposure-mortality pairs were graded "limited-no conclusion." The evidence for other pattern-outcome associations was graded as "limited-no conclusion."

Abbreviations: ACS, American Cancer Society; AICR, American Institute for Cancer Research; CI, confidence interval; CRC, colorectal cancer; CUP, Cancer Update Programme; DIS, dietary inflammation scores; EDIH, Empirical Dietary Pattern for Hyperinsulinemia; ELIH, Empirical Lifestyle Index for Hyperinsulinemia; HLI, Healthy Lifestyle Index; ICVHMs, Ideal Cardiovascular Health Metrics; ICL, Imperial College London; LCA, latent class analysis; LIS, lifestyle inflammation scores; PLFIS, Protective Lifestyle Factor Index Score; PNNS-GS, Programme National Nutrition Santé Guideline Score; RCT, randomized controlled trial; RoB-Nobs, Risk of Bias for Nutrition Observational Studies; ROBINS-I, Risk Of Bias In Non-randomized Studies of Interventions; RR, relative risk; RRR, reduced rank regression; WCRF, World Cancer Research Fund.

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Conclusions: Adopting a healthy pattern of diet, maintaining a healthy weight, staying physically active, and embracing health-conscious habits, such as avoiding tobacco and moderating alcohol, are collectively associated with a lower CRC risk. Healthy lifestyle habits are key to primary CRC prevention. This study was registered at PROSPERO as CRD42022324327 (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022324327)

Keywords: adult, colorectal cancers, dietary patterns, epidemiology, incidences, lifestyle, mortalities, prospective studies, public health, review

Introduction

With over 1.9 million estimated incident cases in 2020, colorectal cancer (CRC) ranked third globally in prevalence and second in cancer-related mortality [1,2]. CRC is influenced by various established modifiable lifestyle risk factors. According to the International Agency for Research on Cancer and the National Cancer Institute, beyond poor diets and alcohol drinking, other lifestyle factors such as physical inactivity and overweight/obesity are linked to an increased CRC risk [3]. On the basis of a global review that included cohort studies and randomized controlled trials (RCTs) up to April 2015, the 2018 Third Expert Report by the World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR), there is "strong—convincing" evidence linking greater processed meat and alcohol consumption, as well as greater adiposity, to increased CRC risk. The report also highlighted physical activity as a factor associated with reduced colon cancer risk [4,5]. Furthermore, cigarette smoking was associated with increased CRC risk [6].

Recent focus has shifted from examining individual risk factors to adopting comprehensive dietary-lifestyle patterns for CRC prevention [4]. Various methods have been used to define dietary-lifestyle patterns in understanding how diet and lifestyle behaviors collectively influence CRC risk [7–9]. A priori methods use existing knowledge of "healthy" diets, lifestyles, and disease risks to create scoring systems that reflect alignment with established dietary-lifestyle recommendations. A posteriori methods use statistical techniques such as factor and cluster analysis to derive patterns from available data. Hybrid methods combine a priori and a posteriori approaches, deriving data-driven patterns to explain the highest variability of a priori selected intermediate factors (for example, biomarker) and target them toward a specific disease.

Despite more studies examining dietary-lifestyle patterns, the 2018 WCRF/AICR reported limited evidence to establish recommendations on whole dietary-lifestyle patterns because of insufficient research and inconsistent pattern definitions [4]. As part of the ongoing Global Cancer Update Programme (CUP Global), formerly known as the WCRF/AICR Continuous Update Project, an updated systematic review was conducted to summarize current evidence on dietary-lifestyle patterns and their association with the risks of CRC, both overall and by anatomic subsite [colon (proximal colon, distal colon) and rectal cancer], and CRC mortality. This updated review improved upon the WCRF/AICR Third Export Report, using a clearer methodology to investigate dietary-lifestyle patterns categorized by the derivation method. The objective of this review was to provide a better understanding of the current state of knowledge including an independent assessment of the strength of the evidence and identify areas that require further investigations.

By focusing on the evidence of dietary-lifestyle patterns, this review complements an accompanying paper, (Chu, 2025; doi: https://doi.org/10.1016/j.ajcnut.2025.02.021.) which investigates dietary patterns exclusively.

Methods

The review protocol is available at https://osf.io/z9naw/. The systematic review was registered in PROSPERO on May 9, 2022 and further updated on July 6, 2023, to extend the literature search up to March 31, 2023 (source: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022324327).

Search strategy

The CUP Global research team at Imperial College London (ICL) conducted searches on PubMed and Embase from database inception up to December 31, 2018 using the WCRF CUP Global search strategy and extracted relevant lifestyle factors and cancer data into the in-house CUP Global database. Search terms are listed in Appendix A. The study selection process involved an initial screening of all titles and abstracts, followed by a thorough examination of full-text articles and reference lists. A subsequent search, employing the same strategy, was conducted for articles published between January 1, 2019 and March 31, 2022, with an extension for articles published up to March 31, 2023.

Study selection

Inclusion criteria involved peer-reviewed studies that investigated: *1*) males and females aged 18 y or older, free of cancer (except non-melanoma skin cancer); *2*) alignment with dietary-lifestyle patterns described by the combination of the dietary pattern and lifestyle risk/behavior factors such as body adiposity, physical activity, alcohol intake, smoking or others, assessed using data-driven, predefined, or mixed methods-defined indices or scores, with details on the components and their cut-off points; *3*) comparison/control groups that aligned with varying dietary-lifestyle patterns, or differing levels of the same pattern; and *4*) incidence or mortality related to CRC. In this article, "mortality" specifically refers to the incidence of fatal CRC in populations initially free of cancer. Types of studies for inclusion were RCTs, prospective cohort studies, nested case-control studies, case-cohort studies, and pooled analyses of studies with these designs. Studies must report relative risk (RR), hazard ratio, or odds ratio along with its corresponding measure of variability. Studies were excluded if published in languages other than English, if participants were under 18 (children/adolescents), if they exclusively involved individuals with diseases (except diabetes) or hospitalized patients because of illness or injury, if participants had prior cancer diagnoses, or if the dietary pattern components were solely based on nutrient intakes. The exclusion of participants with prior cancer diagnoses ensures consistency across studies evaluating both CRC risk and mortality outcomes. Although this exclusion might remove studies derived from CRC patient cohorts examining survival, our focus is specifically on population-based studies assessing "dietary-lifestyle" patterns and their association with the development of fatal CRC, rather than survival after a diagnosis. When multiple publications reported on the same or overlapping populations, the publication with the largest number of events and longer follow-up periods was selected for inclusion.

Data extraction

The following data were extracted from each study: *1*) the first author's last name, year of publication, and country; *2*) study name, design, and participant characteristics; *3*) number of cases, study sample size, and follow-up period; *4*) case ascertainment method; *5*) method for exposure assessment, including the name and a brief description of each pattern including its components; *6*) types of outcome (incidence or mortality; cancer site); *7*) RR estimates with their corresponding 95% confidence intervals (CI) or *P* values for the exposure comparisons; and *8*) variables included in any adjusted analyses. A second reviewer independently assessed ≥10% of the study selection and conducted data extraction. Any discrepancies were resolved by consensus through discussion.

Risk-of-bias assessment

The risk of bias in each included study was evaluated and graded according to pre-established criteria, using a modified version of the Risk of Bias for Nutrition Observational Studies (RoB-NObs) tool (Appendix B). The RoB-NObs tool was originally developed by the United States Department of Agriculture Nutrition Evidence Systematic Review [10], based on modifications to the Cochrane's collaboration Risk Of Bias In Non-randomized Studies of Interventions [11]. The RoB-NObs tool (version dated March 9, 2022) was optimized and tested by the ICL review team, and additional confounding factors were incorporated for further adaptation (Appendix B). Seven domains are covered for the observational studies: *1*) confounding, *2*) participant selection, *3*) exposure classification, *4*) departure from intended exposures, *5*) missing data, *6*) outcome measurement, and *7*) selection of reported results.

Data synthesis

Studies were categorized according to methods used to derive dietary-lifestyle patterns: *1*) a priori patterns based on specific recommendations for cancer prevention, *2*) a priori patterns based on general recommendations for a healthy lifestyle, *3*) a posteriori patterns, and *4*) hybrid patterns.

All studies were summarized narratively. Meta-analysis was not performed to summarize the results because the identified patterns within groups were heterogeneous in terms of components and cut-off points. The approach undertaken involved summarizing measures of associations using descriptive statistics (range) and vote counting based on the direction of reported associations (null, positive, or inverse), which was applied after grouping studies based on predefined characteristics (types of patterns, outcome). A descriptive synthesis was conducted separately for each investigation of dietary-lifestyle patterns with the risk of all CRC combined, colon cancer, rectal cancer, colon cancer subsites [proximal (or right-sided) colon cancer, distal (or left-sided) colon cancer] and CRC mortality.

Forest plots were generated (for patterns investigated in a minimum of 3 studies) to visually present all the data and facilitate a narrative summary. The forest plots present RR estimates and 95% CIs for comparisons between the highest and lowest exposure categories, without calculating an overall summary effect. For studies comparing the lowest with the highest exposure categories, an inversion of the effect estimates was performed. When studies reported separate RR estimates for each outcome category (total CRC, colon cancer, rectal cancer, or colon subsites) within subgroups (for example, females or males), and overall population data were unavailable, we used a fixed-effect model to pool the estimates and calculate an overall estimate for each outcome category (marked with an "*" in the forest plots). These pooled estimates were then included in the descriptive evidence synthesis with other studies. For studies reporting only continuous (linear dose–response) associations, the results are presented in Supplemental Tables 1–4 and within the text.

For a priori dietary-lifestyle patterns, we explored potential sources of heterogeneity by performing predefined subgroup/sensitivity analyses (when ≥2 studies were available in each subgroup), presenting forest plots to visually assess the range of RRs and their 95% CIs across studies. The subgroups investigated were as follows: sex (females and males), geographical location of the studies by continent (North America, Europe, and Asia), and smoking (included or not as a score component).

Although a meta-analysis was not feasible, we assessed potential small-study effects, such as publication bias, by using visual inspection of funnel plots and Egger's regression asymmetry test for patterns with ≥10 included studies [12]. Statistical analyses were conducted using Stata 18 (StataCorp).

Grading the quality-of-evidence

The quality-of-evidence was evaluated and graded independently by the CUP Global Expert Committee on Cancer Incidence and Expert Panel according to the predefined WCRF/AICR evidence grading criteria (Supplemental Table 5) [13]. Grades indicating strong evidence (with subgrades for likelihood of causality: convincing, probable, or substantial effect on risk unlikely) or limited evidence (with subgrades for likelihood of causality: "limited—suggestive" or "limited—no conclusion") were assigned. Factors considered in the evaluation and grading were quantity, consistency, magnitude, and precision of the summary estimates, presence of a dose–response relationship, study design and risk of bias, generalizability, and mechanistic plausibility of the results.

Results

Figure 1 presents a flow diagram depicting the study selection process. A total of 27,464 publications retrieved from the new searches (for articles between 2019 and 2023) were screened, identifying 28 additional publications. Major reasons for exclusion were that the publication type or study design did not align with the specified inclusion criteria. We also excluded studies that were outside the scope of the research topic, such as those on nutrient-based dietary patterns [14–21], organic food consumption [22], ultraprocessed food intake [23], and specific eating behaviors [24]. Combining these 28 publications with 48 articles retrieved from the CUP Global database resulted in 76 publications on dietary and lifestyle patterns. After excluding 43 publications that did not assess lifestyle patterns, 33 publications investigating combined dietary-lifestyle patterns were included in this review [25–57].

Study characteristics

The dietary-lifestyle patterns evaluated are a combination of diets with other risk factors or behavioral patterns, such as adiposity, physical activity, alcohol consumption, or smoking. No RCTs were identified. All studies included were observational, with detailed results and main characteristics presented in Supplemental Tables 1–4.

Among the total 33 identified publications published between 2012 and 2023, 29 (26 prospective cohorts, 2 pooled analyses of cohorts, and 1 nested case-control study) used a priori-derived scores [25–53], 1 (prospective cohort) used a posteriori derived scores [54], and 3 (2 prospective cohorts and 1 pooled analysis of cohorts) used

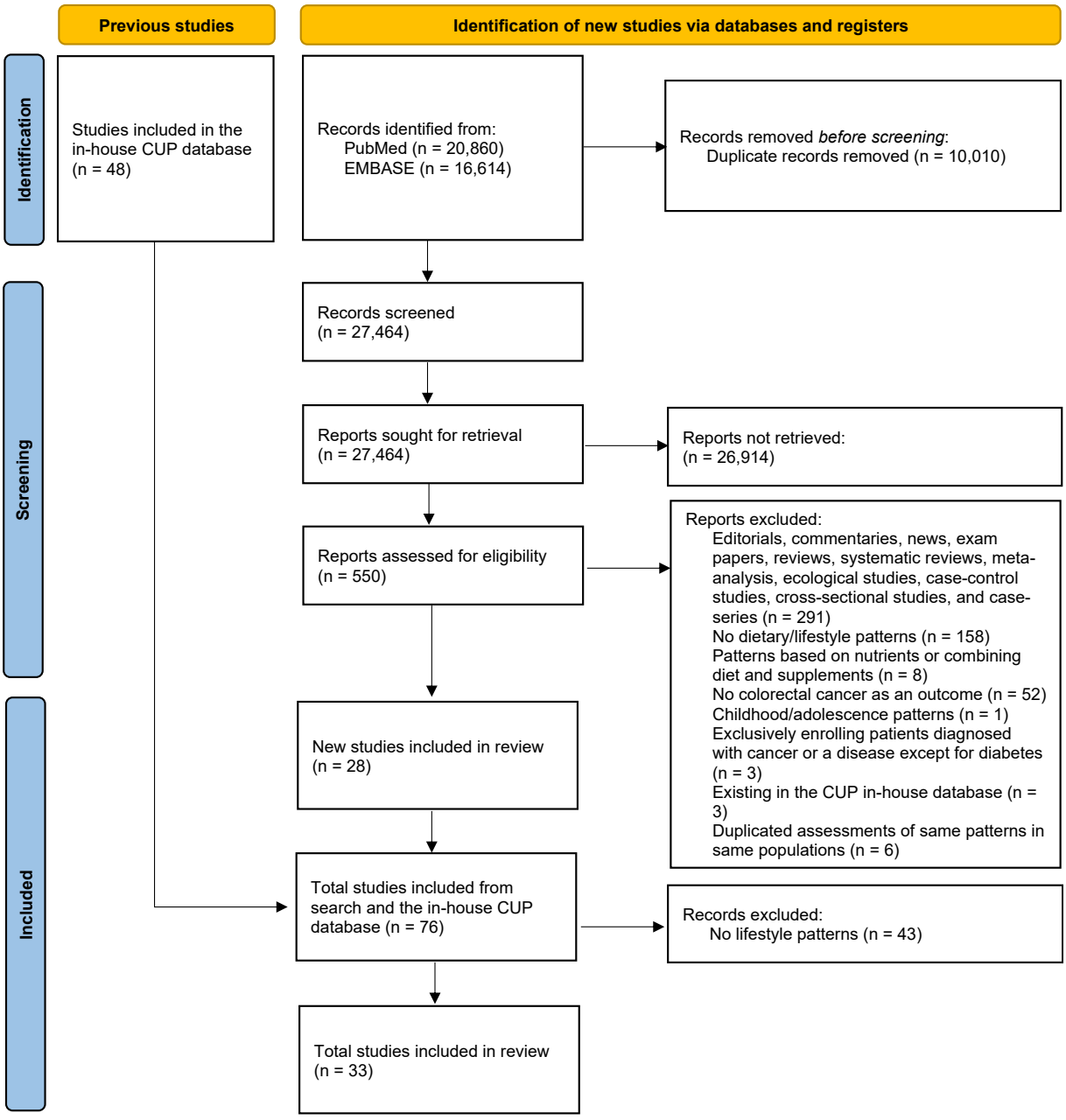

FIGURE 1. PRISMA flow chart of study selection. CUP Global, Global Cancer Update Programme.

hybrid-derived scores [55–57]. Studies were mostly conducted across Europe (n=14) [25–27,29,30,32,35,36,39,43,47–49,53] and North America (n=15) [28,31,33,34,37,38,40–42,44,51,54–57], with 3 from Asia [45,46,52], and 1 spanning North America, Europe, and Asia [50]. Cohort sizes ranged from 2983 [42] to 476,396 [41] participants (median: 72,695), and the number of diagnosed CRC cases ranged from 53 [45] to 10,702 [48] (median: 860). Twenty-one studies had follow-up durations >10 y [25,28–30,33–35,37,39–44,46,47,51,54–57] and 12 had ≤10 y [26,27,31,32,36,38,45,48–50,52,53], with a median follow-up duration of ~12.3 y across all studies.

Risk-of-bias assessment

A summary of the risk-of-bias assessment for the studies is presented in Appendix C. Approximately 60% of studies presented serious-to-critical bias related to confounding (study biased because of either unadjusted or nonvalidated key confounders, including energy intake, socioeconomic status, etc.) A detailed list of all confounders is available in Appendix C. Note that adjustment for alcohol, smoking, physical activity, and BMI was mandatory if these were not already included as exposure variables. 88% had moderate participant selection bias (with no studies presenting serious or critical bias); 24% presented serious bias in exposure classification (primarily because of a lack of validation and replication data for self-reported measurements or lack of lag time analysis); 88% had critical bias because of departure of intended exposures (as most studies examined dietary-lifestyle factors only once at baseline, without considering possible fluctuations during follow-up); 24% had serious bias in handling missing data (mainly because proportions of missing participants differed substantially across exposures); 15% had serious bias in outcome measurement (authors reported some differences in outcome ascertainment), and lastly, all studies had moderate bias in the

TABLE 1
Evidence grades and main findings from the descriptive synthesis of dietary-lifestyle patterns and colorectal cancer risk/mortality.

Evidence grades	Pattern	Colorectal cancer or subsites	Summary of findings	Conclusions
Decreases risk				
Strong evidence Probable	A priori dietary-lifestyle patterns based on specific recommendations for cancer prevention (WCRF/AICR score)	CRC	For the highest vs. lowest level of alignment, 13 RRs (from 12 publications) ranged 0.39–0.96: 6/13 RRs 95% CIs excluded 1 For each 1-unit increment in the score, 3 RRs (from 3 publications) ranged 0.85–0.93: 1/3 RRs 95% CIs excluded 1	Evidence based on overall consistent trend of inverse associations. No evidence of publication bias, with a consistent direction when measured across continents. Scores formed from components with strong mechanistic evidence.
		Colon cancer	For the highest compared with lowest level of alignment, 5 RRs (from 4 publications) ranged 0.54–0.84: 2/5 RRs 95% CIs excluded 1 For each 1-unit increment in the score, 1 RR (95% CI): 0.93 (0.85, 1.02)	Evidence based on overall consistent trend of inverse associations. No evidence of publication bias. Scores formed from components with strong mechanistic evidence.
Limited evidence				
Suggestive	A priori dietary-lifestyle patterns based on specific recommendations for cancer prevention (ACS score)	CRC	For the highest vs. lowest levels of alignment, 4 RRs (from 4 publications) ranged 0.48–0.88: 2/4 RRs 95% CIs excluded 1	Evidence based on consistent trend of inverse associations. No evidence of publication bias. Supported by plausible mechanistic evidence for pattern components. Some risk of bias concerns because of confounding in studies.
	A priori dietary-lifestyle patterns based on general recommendations for a healthy lifestyle [Healthy Lifestyle Index (and modifications)]	CRC	For the highest vs. lowest levels of alignment, 4 RRs (from 4 publications) ranged 0.50–0.66: all RRs 95% CIs excluded 1	Evidence based on consistent trend of inverse associations. No evidence of publication bias. Supported by plausible mechanistic evidence for pattern components. Substantial risk of bias concerns because of confounding in studies.
Increases risk				
Strong evidence Probable	Hybrid dietary-lifestyle patterns derived from biological markers (Empirical Lifestyle Index for Hyperinsulinemia)	CRC	For the highest vs. lowest levels of alignment, 3 RRs (from 2 publications) ranged 1.28–1.74: all RRs 95% CIs excluded 1	Evidence based on overall consistent trend of positive associations. No evidence of publication bias. Supported by plausible mechanistic evidence for pattern components.
No conclusion				
Limited evidence No conclusion	A priori dietary-lifestyle patterns based on specific recommendations for cancer prevention:WCRF/AICR score (rectal cancer risk and CRC mortality), ACS score (colon cancer risk, rectal cancer risk, and CRC mortality), Healthy Lifestyle Index and Protective Lifestyle Factor Index Score (CRC, colon cancer, and rectal cancer risks)			The evidence is based on 2 or more estimates from cohort studies or pooled analyses but showing inconsistency in the associations.
	A priori dietary-lifestyle patterns based on general recommendations for a healthy lifestyle: Healthy Lifestyle Index (colon cancer and rectal cancer risks), Evolutionary-concordant diet + lifestyle score (CRC risk), Programme National Nutrition Santé Guideline Score (CRC risk), Ideal Cardiovascular Health Metrics (CRC risk) Hybrid dietary-lifestyle patterns derived from biological markers: Lifestyle inflammation scores + dietary inflammation scores (CRC risk), Empirical Lifestyle Index for Hyperinsulinemia (colon and rectal cancer risks)			The evidence is based on 1 estimate from a cohort study or pooled analysis.
	A posteriori dietary-lifestyle patterns based on cluster analysis: High-risk classes (CRC risk)			The evidence is based on 2 or more estimates from a single cohort study.

Abbreviations: ACS, American Cancer Society; CI, confidence interval; CRC, colorectal cancer (which includes both colon cancer and rectal cancer combined); RR, relative risk; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.
Note: the level of confounding between exposure-outcome pairs is categorized as follows:
- Moderate confounding in all studies: Some risk of bias (RoB).
- Moderate and serious confounding in studies: RoB concerns.
- Critical confounding for RoB in studies: Substantial RoB concerns.

selection of reported result (because of the absence of preregistered protocols or analysis plans, a common issue in observational studies).

Evidence grading

Table 1 shows the summary findings and the judgment of the CUP Global Expert Committee on Cancer Incidence and Expert Panel. A visual summary of the quality-of-evidence matrix is presented in Figure 2. Detailed judgments on the evidence concluded for a priori patterns are provided in Supplemental Table 6 (based on specific recommendations for cancer prevention) and Supplemental Table 7 (based on general recommendations for a healthy lifestyle); and for hybrid patterns in Supplemental Table 8. Grading of the evidence for a posteriori patterns is not provided because of limited studies (only 1 study), but the results and main characteristics of the study are available in Supplemental Table 3.

Results					
Summary of evidence matrix	**Dietary-lifestyle patterns**	**CRC risk**	**Colon cancer risk**	**Rectal cancer risk**	**CRC mortality**
A priori					
Cancer prevention recommendations	WCRF/AICR recommendations score				
	American Cancer Society (ACS) guidelines				
	Healthy Lifestyle Index (HLI) & Protective Lifestyle Factor Index Score (PLFIS)				
General healthy lifestyle recommendations	Healthy Lifestyle Index (HLI) (& modifications)				
	Evolutionary-concordant diet + lifestyle score				
	Programme National Nutrition Santé Guideline Score (PNNS-GS)				
	Ideal Cardiovascular Health Metrics (ICVHMs)				
A posteriori					
Based on cluster analysis	High-risk classes				
Hybrid					
Derived from biological markers	Empirical Lifestyle Index for Hyperinsulinemia (ELIH) (& modifications)				
	Lifestyle inflammation scores (LIS) + Dietary inflammation scores (DIS)				

Conclusions key

Decreases risk: Strong – Convincing; Strong – Probable; Limited – Suggestive

Limited – No conclusion

Increases risk: Limited – Suggestive; Strong – Probable; Strong – Convincing

Note: Empty (white) cells represent exposure-outcome pair not reviewed and no evidence grading assigned.

FIGURE 2. Summary quality-of-evidence matrix from the systematic literature review on alignment with dietary-lifestyle patterns and colorectal cancer outcomes. CRC, colorectal cancer; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.

Pattern group	Pattern name	No. of papers	Score versions	Characteristic											
				Adiposity	Physical activity	Smoking	Alcohol	Fruits	Vegetables	Legumes	(Whole) grains and cereals/fiber	Dairy products	Red meat/processed meat	Sugar-sweetened beverages	Sodium
"*A priori*" dietary-lifestyle patterns															
Based on specific recommendations for cancer prevention	WCRF/AICR recommendations score	16	16	16	15	2	15	16	16	4	11		14	9	6
	American Cancer Society (ACS) guidelines	5	5	5	5	2	3	5	5		4		5		
	Healthy Lifestyle Index (HLI) and Protective Lifestyle Factor Index Score (PLFIS) for cancer prevention	3	3	3	3	3	3	3	3	1	2	2	3	1	
Based on general recommendations for a healthy lifestyle	Healthy Lifestyle Index (HLI) (and modifications) for a healthy lifestyle	4	4	4	4	4	3	4	4	1	2	2	3	1	2
	Evolutionary-concordant diet + lifestyle score	1	1	1	1	1	1	1	1		1	1	1	1	1
	Programme National Nutrition Santé Guideline Score (PNNS-GS)	1	1		1		1	1	1	1	1	1		1	1
	Ideal Cardiovascular Health Metrics (ICVHMs)	1	1	1	1	1		1	1		1		1		
"*A posteriori*"															
Based on cluster analysis	High risk classes[1]	1	17	7	4	7	5	1	1				5		
Hybrid															
Derived from biological markers	Empirical Lifestyle Index for Hyperinsulinemia (ELIH) (& modifications)[1]	2	2	1	1		2	2	1			2	2	1	
	Lifestyle inflammation scores (LIS) + Dietary inflammation scores (DIS)[1]	1	1	1	1	1	1	1	1	1	1	1	1	1	

FIGURE 3. Summary of components of dietary-lifestyle patterns. WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research. Dark green indicates higher exposure values in most patterns (≥50% of score versions); light green indicates higher exposure values in some patterns (between 2% and 50% for patterns with ≥4 score versions, or 1% if 3 score versions for that pattern). Dark red signifies lower exposure values in most patterns, whereas light red denotes lower exposure values in some patterns. Yellow signifies moderate exposure values in most patterns. [1]For comparability, the pattern alignment in this figure was reversed to indicate a healthy dietary-lifestyle direction.

A priori patterns

A priori patterns were categorized into 2 main groups based on whether the scores reflected: *1*) specific recommendations for cancer prevention, or *2*) general recommendations for maintaining a healthy lifestyle. Some common components shared by these 2 scores were healthy weight, physical activity, moderate to no alcohol consumption, and following a healthy diet (Figure 3). All studies assessed CRC risk as an outcome, and 1 study assessed only CRC mortality [39]. Ten publications investigated CRC risk at different subsites: colon, rectal, proximal colon, and distal colon cancer [27,28,33–35,40,41,43,46,52] (Figure 4 and Supplemental Figure 1).

In 27 associations investigating all a priori patterns based on categorical comparisons of exposures and CRC risk, one-third (33%) showed null association, slightly less than half (44%) showed moderate inverse associations (RRs ranging from 0.51 to 0.80) and around a quarter (22%) showed strong inverse associations (RRs ranging from 0.25 to 0.50). Of note, among a priori patterns, studies with null findings or moderate associations showed a higher prevalence of serious-to-critical bias because of confounding (presented in 20% of null findings and nearly 30% of moderate associations; compared with only 4% of studies with strong associations).

Within all a priori dietary-lifestyle patterns, subgroup analysis by sex showed no clear sources of heterogeneity in the associations between alignment with the dietary-lifestyle patterns and CRC/colon cancer risk (Supplemental Figure 2). Notably, for rectal cancer, higher alignment with the Healthy Lifestyle Index (HLI) showed a lower risk in males [RRs (95% CIs): 0.35 (0.24, 0.52) and 0.47 (0.32, 0.68)], whereas females showed no clear association [RR: 1.01 (0.68, 1.49)]. However, it is important to note that there is a limited number of studies investigating this sex-specific association. No clear sources of heterogeneity were observed by geographical region (Supplemental Figures 3). Studies that included smoking component in a priori scores showed stronger associations compared with studies without a smoking component, as evident by a greater number of studies with smoking component excluded null associations for CRC risk, and stronger effect size estimates for rectal cancer risk [that is, HLI with smoking component: 0.35 (95% CI: 0.24, 0.52) compared with the American Cancer Society (ACS) guidelines without smoking component: 0.61 (0.53, 0.71); Supplemental Figure 4]. No strong evidence of small-study effects (that is, publication bias) was observed for all a priori patterns ($P = 0.908$; Supplemental Figure 5).

A priori patterns based on specific recommendations for cancer prevention

Twenty-three publications from 19 individual observational studies [25–38,40–47] and 1 pooled cohort analysis [39] assessing a priori patterns based on specific recommendations for cancer prevention were identified. Two main types of scores were used: the WCRF/AICR recommendations (16 publications [25–27,31–40,42,45,47]), and the ACS scores (5 publications [26,28,29,41,44]) (Figure 3). One publication investigated both the WCRF/AICR recommendations and the ACS guidelines [50]. Most studies assessed the 2007 WCRF/AICR recommendations [27,31,35–40,42,45,47], whereas 5 assessed the updated 2018 WCRF/AICR recommendations [25,26,32–34]. Common components between 2007 and 2018 WCRF/AICR recommendations included maintaining a healthy weight, being physically active, following a healthy diet rich in fruits, vegetables, and whole grains while limiting red/-processed meat, sugar-sweetened beverages, and alcohol consumption.

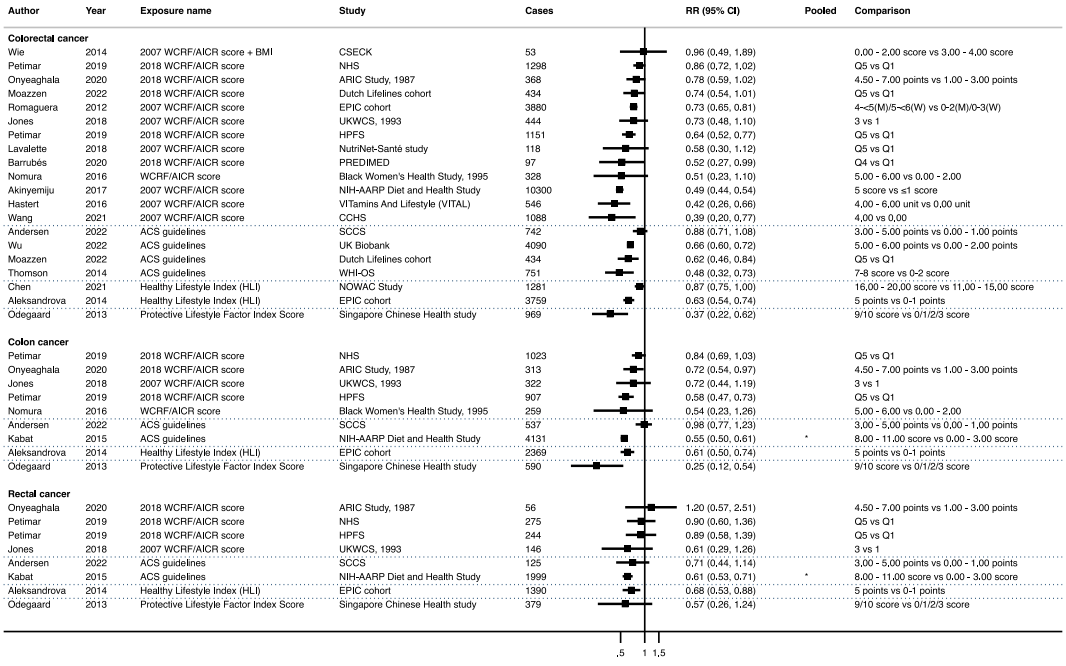

FIGURE 4. RR (95% CI) of colorectal cancer incidence for the highest compared with the lowest level of alignment with "a priori" dietary-lifestyle patterns based on specific recommendations for cancer prevention. The blue-dotted horizontal reference lines indicate distinct dietary pattern groups. *Pooled estimates from subgroup RRs reported in the publications, calculated using a fixed-effect model before being presented in the forest plot. ACS, American Cancer Society; ARIC, Atherosclerosis Risk in Communities; CCHS, Canadian Community Health Survey; CI, confidence interval; CSECK, Cancer Screening Examination Cohort, Korea; EPIC, European Prospective Investigation into Cancer and Nutrition; HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; NOWAC, Norwegian Women and Cancer Study; PREDIMED, PREvención con Dieta MEDiterránea; RR, relative risk; SCCS, Southern Community Cohort Study; UKWCS, UK Women's Cohort Study; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research; WHI-OS, Women's Health Initiative—Observational Study.

Five studies based on either the 2007 or 2018 WCRF/AICR recommendations additionally included tobacco smoking into the scores [25,28,29,31,37]. Two studies [30,43] investigated HLI for cancer prevention and 1 study investigated Protective Lifestyle Factor Index Score (PLFIS) [46]. Sleep was included in lifestyle scores by 2 studies: one based on the ACS guidelines [29], and another based on the PLFIS [46].

Most studies examining dietary-lifestyle patterns based on specific recommendations for cancer prevention found an inverse direction of association with CRC, colon, and rectal cancer risk (Figure 4; detailed results and characteristics for both categorical and continuous/linear dose–response associations are presented in Supplemental Table 1). The evidence for the association between alignment with the WCRF/AICR recommendations for cancer prevention and a lower risk of CRC was graded as "strong—probable." All studies consistently showed an inverse direction of association with CRC risk (13 associations, RRs for the highest compared with the lowest category ranged from 0.39 to 0.96; in 6 associations 95% CIs excluded 1). Three studies examined only the linear dose–response associations [25,27,42], all of which reported an inverse direction of association between alignment with the 2007 [RR (95% CI) per 1-point increase: 0.87 (0.68, 1.12) and 0.93 (0.86, 1.00)] and 2018 WCRF/AICR recommendations [RR (95% CI) per SD increase: 0.85 (0.82, 0.89)] and CRC risk. Similarly, the evidence for alignment with the WCRF/AICR recommendations and colon cancer risk was graded as "strong—probable" (5 associations, RRs ranged from 0.54 to 0.84; in 2 associations 95% CIs excluded 1).

For colon cancer subsites, 3 associations between alignment with WCRF/AICR recommendations and proximal colon cancer reported RRs ranging from 0.82 to 0.83 (all 95% CIs included 1); and 3 associations with distal colon cancer reported RRs ranging from 0.41 to 0.83 (in only 1 association the 95% CIs excluded 1; Supplemental Figure 1) [34,35]. One study [27] examined the linear dose–response associations (per 1-point increment with the WCRF/AICR score) with colon [RR (95% CI): 0.93 (0.85, 1.02)], proximal colon [RR: 1.00 (0.87, 1.14)], and distal colon [RR: 0.89 (0.79, 1.01)] cancer risk (Supplemental Table 1). In sex-stratified analysis, among males, 4 associations between alignment with WCRF/AICR recommendations and CRC risk reported RRs for the highest compared with the lowest category ranging from 0.27 to 0.86 (in 3 associations 95% CIs excluded 1); in females, 6 associations reported RRs ranging from 0.45 to 0.86 (in 2 associations the 95% CIs excluded 1; Supplemental Figure 2).

The evidence for the association between alignment with the ACS guidelines score for cancer prevention and a lower CRC risk was graded as "limited—suggestive" (4 associations, RRs ranged from 0.48 to 0.88; in 3 associations 95% CIs excluded 1) mainly because of the lack of adjustment for required confounders (for example, sex, energy intake) in some studies. No studies examined the association between alignment with the ACS guidelines score and proximal/colon cancer. The evidence for the remaining associations [that is, WCRF/AICR recommendations (for rectal cancer risk), ACS guidelines (for colon and rectal cancer risk), HLI for cancer prevention, and PLFIS (for CRC, colon, and rectal cancer risk)] was limited and sparse; thus, graded as "limited—no conclusion."

There was "limited—no conclusion" evidence for CRC mortality. Two studies investigating WCRF/AICR recommendation scores and CRC mortality reported RRs (95% CI) of 0.80 (0.50, 1.26) [33] and 0.84 (0.50, 1.42) [39] over a mean follow-up of 22–23 y; another study investigating ACS guidelines score and CRC mortality reported RR of 0.39 (0.24, 0.63) over a mean follow-up of 13 y [44] (Supplemental Table 1).

A priori patterns based on general recommendations for a healthy lifestyle

Seven publications from 4 individual observational studies [36,48,49,51–53] and 1 pooled cohort analysis [50] exploring dietary-lifestyle patterns based on general recommendations for a healthy lifestyle and CRC risk were included in this review (Supplemental Table 2). Four main dietary-lifestyle patterns were assessed: HLI for a healthy lifestyle [48,50,52,53], combined evolutionary-concordance diet and lifestyle score [51], French National Nutrition Health Program-Guideline Score (PNNS-GS) [36], and Ideal Cardiovascular Health Metrics (ICVHMs) [49]. Common components of these patterns are physical activity and a diet rich in fruits and vegetables (Figure 3).

The evidence of alignment with HLI for a healthy lifestyle with CRC risk was graded as "limited—suggestive" (4 associations, RRs for the highest compared with the lowest category ranged from 0.50 to 0.66; in all associations 95% CIs excluded 1; Figure 5), primarily attributed to the lack of adjustment for required (for example, energy intake) and/or desirable confounders (for example, comorbidities, prior endoscopy/colonoscopy) in the studies; hence, the evidence was insufficient to support a grading higher than "limited—suggestive."

The evidence for the remaining associations [that is, HLI for a healthy lifestyle (for colon and rectal cancer risk), evolutionary-concordant diet and lifestyle score (for CRC risk), PNNS-GS (for CRC risk), ICVHMs (for CRC risk)] was graded as "limited—no

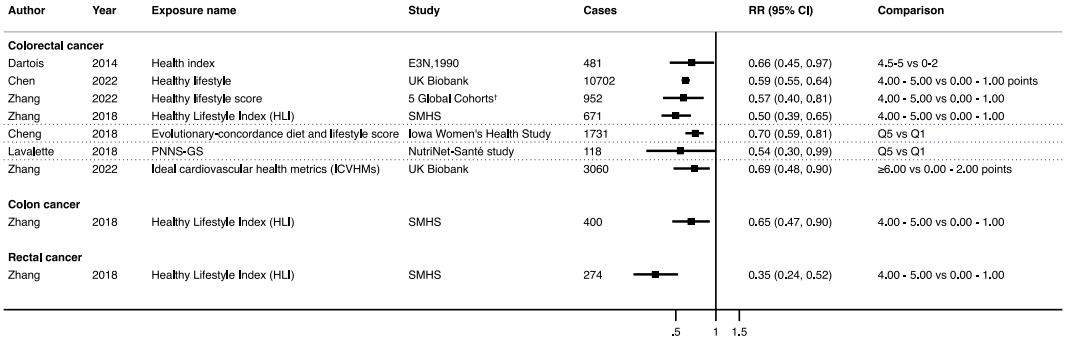

FIGURE 5. RR (95% CI) of colorectal cancer incidence for the highest compared with the lowest level of alignment with "a priori" dietary-lifestyle patterns based on general recommendations for a healthy lifestyle. The blue-dotted horizontal reference lines indicate distinct dietary pattern groups. †Five Global Cohorts included the National Health and Nutrition Examination Survey, National Institutes of Health-American Association of Retired Persons Diet and Health Study, the UK Biobank study, Dongfeng-Tongji cohort, and Kailuan study. CI, confidence interval; HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; PNNS-GS, Programme National Nutrition Santé Guideline Score; RR, relative risk; SMHS, Shanghai Men's Health Study.

conclusion" because of the scarcity of studies, with only 1 study available for each pattern.

A posteriori dietary-lifestyle patterns

A posteriori patterns were only investigated in one prospective cohort study [54] from the Alberta's Tomorrow Project using latent class analysis (LCA) (median follow-up: 13.2 y). This study comprised 26,460 participants and identified 267 CRC cases (Supplemental Table 3).

The evidence for a posteriori dietary-lifestyle patterns and CRC risk was graded as "limited—no conclusion." The study [54] identified 7 patterns (classes) with varying CRC risk factors. Compared with the low-risk class ("Class 2"; non-smoking, normal weight, but low vegetable intake), 6 high-risk classes showed RRs ranging from 1.56 to 2.87. Of the 6 high-risk classes, 4 were associated with an increased CRC risk compared with "Class 2" (reference group), namely: "Class 1"; characterized by high meat/low vegetables intake [RR (95% CI): 2.48 (1.27, 4.83)], "Class 4"; featuring low meat/high fruit and vegetable intake, physical inactivity, and overweight/obesity [RR: 2.34 (1.23, 4.45)], "Class 5"; with an obese BMI and alcohol avoidance [RR 2.46 (1.28, 4.70)]; and "Class 7"; with multiple risk factors—current smokers, high-risk alcohol consumption, and physical inactivity [RR: 2.87 (1.43, 5.77)]. The remaining 2 classes that did not show strong evidence of an increased risk were as follows: "Class 3"; characterized by low meat consumption, high physical activity levels, normal BMI, and current or former smokers [RR: 1.56 (0.79, 3.06)], and "Class 6"; comprising former smokers, high-risk drinkers, high physical activity levels, and overweight [RR: 1.73 (0.85, 3.49)].

Hybrid dietary-lifestyle patterns

Three publications from 4 observational studies from North America used hybrid methods to derive patterns most predictive of C-peptide [55,57] or inflammatory biomarkers [56] (Figure 3 and Supplemental Table 4). Cohort sizes in these studies ranged from 94,217 to 453,465 participants, with observed cases of CRC ranging from 332 to 10,336, ascertained from 13.5 to 24 y of follow-up.

Two dietary-lifestyle patterns, either related to hyperinsulinemia or proinflammatory, were examined for their association with CRC risk: *1*) the Empirical Lifestyle Index for Hyperinsulinemia (ELIH) [55,57], and *2*) a combination of inflammation biomarker panel-weighted lifestyle inflammation scores (LIS) and whole food-based dietary inflammation scores (DIS) [56], computed as a composite of diet, BMI, and physical activity.

Evidence for a higher alignment with ELIH and an increased CRC risk was graded as "strong—probable" (3 associations, RRs ranged from 1.28 to 1.74, in all associations 95% CIs excluded 1; Figure 6). Only 1 study [55] explored the ELIH and CRC risk by anatomical subsite, reporting linear dose–response associations for distal colon and rectal cancer combined [RR (95% CI): 1.64 (1.10, 2.44)], proximal colon cancer [RR: 1.15 (0.65, 2.03)], distal colon cancer [RR: 1.91 (1.09, 3.34)], and rectal cancer [RR: 1.41 (0.82, 2.44)] risks.

One study [56] investigated the combined LIS and DIS, reporting an increased CRC risk [RR (95% CI): 1.83 (1.68, 1.99); Figure 6]. However, because of the limited number of studies, the evidence was graded as "limited—no conclusion."

Discussion

This review updates the evidence on dietary-lifestyle patterns—a priori, a posteriori, hybrid-defined—and CRC risk/mortality. Higher alignment with a priori patterns based on cancer prevention recommendations: WCRF/AICR recommendations were graded "strong—probable" for lower CRC and colon cancer risks, whereas ACS guidelines were graded "limited—suggestive" for lower CRC risk. A priori patterns based on a general healthy lifestyle, HLI, were graded "limited—suggestive" for lower CRC risk. A posteriori patterns were graded "limited—no conclusion" because of insufficient data, with only 1 study included. The hybrid-derived hyperinsulinemic ELIH pattern was graded "strong—probable" for higher CRC risk. Evidence for CRC mortality (for example, WCRF/AICR, ACS) was graded "limited—no conclusion" because of limited studies and imprecise estimates. For other pattern-outcome associations, the evidence was "limited—no conclusion."

Most a priori studies investigated WCRF/AICR scores, although slight scoring variations limited comparisons. Our findings align with reviews showing inverse associations of the 2007 [58] and 2018 WCRF/AICR recommendations [59] on CRC risk. The 2007 WCRF/AICR Second Expert Report [60] outlined 10 cancer prevention recommendations, incorporating body weight, physical activity, diet, and lactation, with updates in 2018 [61]. The 2018 WCRF/AICR updates refined distinctions for high-calorie foods/sugary drinks, removed the sodium recommendation, and noted cancer risks at any alcohol level. Although WCRF/AIRC-based dietary-lifestyle patterns and CRC risk were graded "strong—probable," dietary patterns alone were graded "limited—no conclusion" (described in the accompanying dietary-patterns article), (Chu, 2025; doi: https://doi.org/10.1016/j.ajcnut.2025.02.021.) reflecting the broader impact of dietary-lifestyle patterns on CRC risk through various mechanisms [62–65].

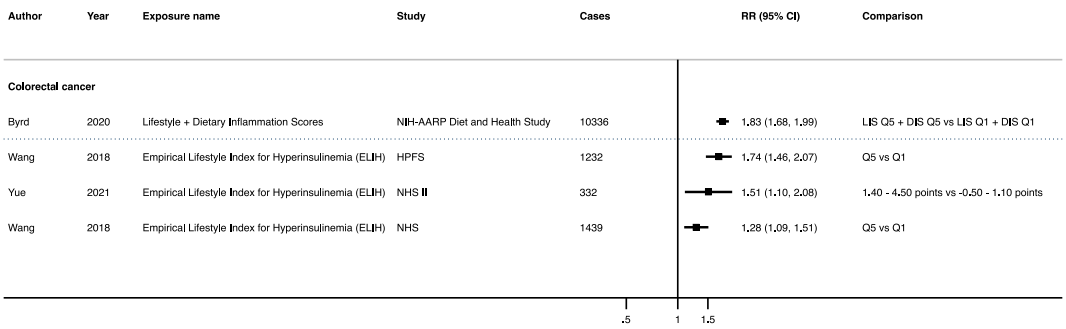

FIGURE 6. RR (95% CI) of colorectal cancer incidence for the highest compared with the lowest level of alignment with hybrid dietary-lifestyle patterns. CI, confidence interval; DIS, dietary inflammation scores; HPFS, Health Professionals Follow-Up Study; LIS, lifestyle inflammation scores; NHS, Nurses' Health Study; RR, relative risk.

Other well-studied a priori-defined patterns, including ACS cancer-specific guidelines and HLI scores, overlap with WCRF/AICR recommendations but emphasize higher dairy intake and lower sodium in the HLI. Dairy may protect against CRC [4] but is excluded from WCRF/AICR recommendations because of potential prostate cancer risk [50]. Nonetheless, dairy is often linked to lower CRC risk [66–68]. Including smoking in lifestyle scores strengthened CRC (and rectal cancer) associations, highlighting the importance of assessing tobacco use [6,69]. Studies incorporating sleep into dietary-lifestyle scores (ACS [29] and PLFIS [46]) showed stronger inverse associations with CRC risk [46]. Collectively, alignment with healthy lifestyle practices—maintaining a healthy weight, physical activity, a healthy diet, limiting alcohol, avoiding smoking, and good sleep—was associated with lower CRC risk.

One study employed a posteriori LCA in Alberta's Tomorrow Project [54], identifying behavioral profiles linked to CRC risk, including obesity, inactivity, red/processed meat, alcohol, smoking, and fruit-vegetable intake. The study [54] highlighted physical activity's role in mitigating CRC risk, particularly for individuals with obesity, aligning with prior findings [70]. Further research assessing regional variations, cultural dietary-lifestyle habits, and food availability on CRC risk is needed.

The hybrid approach provided "strong—probable" evidence linking the hyperinsulinemic ELIH pattern with increased CRC risk. This index, incorporating diet, BMI, and physical activity, highlights the insulinemic potential of lifestyle factors [71]. The accompanying article on dietary patterns also graded the Empirical Dietary Pattern for Hyperinsulinemia and CRC link as "strong—probable." (Chu, 2025; doi: https://doi.org/10.1016/j.ajcnut.2025.02.021.) Notably, evidence suggests stronger associations between insulin/inflammatory-related diets/lifestyle behaviors and cardiometabolic endpoints in African American and Hispanic participants than in the NHS ("replication cohorts") [72,73], possibly because of their predisposition to insulin resistance (for example, obesity). These associations may be underestimated in the NHS and HPFS cohorts because of their relatively health-conscious nature.

CRC risk associations varied by anatomical location. Only the 2018 WCRF/AICR recommendations showed inverse trends with colon and distal colon cancers, but not with rectal/proximal colon cancer. These variations may stem from differences in anatomy [74,75], gut microbiota [76], and metabolite exposure [77]. Sex-specific analyses suggest stronger HLI associations with lower rectal cancer risk in males, potentially because of interactions between sex hormones [78], gut microbiota [79], and site-specific cancer susceptibilities.

Evidence on dietary-lifestyle patterns and CRC mortality is limited. Nonetheless, inverse associations between a priori dietary-lifestyle patterns and CRC incidence suggest potential reductions in CRC mortality, supporting the use of mortality data as a proxy when incidence data are scarce [80]. Although CRC mortality data in this review primarily reflect baseline patterns from healthy cohorts, any behavioral changes post diagnosis were not considered, which may influence survival. However, because most CRC mortality occurs within 5 y post diagnosis, with fatal CRC risk factors largely overlapping those for incident CRC [81], addressing these common determinants is vital for reducing CRC incidence and mortality.

Proposed mechanisms linking dietary-lifestyle factors to CRC highlight insulin signaling as a key pathway [82]. Hyperinsulinemia may promote CRC by stimulating cell growth and inhibiting apoptosis [83–86]. Mendelian randomization studies associated higher fasting insulin with increased CRC risk [87]. Diets rich in refined carbohydrates, sugary drinks, and low in fiber can impair blood sugar control, leading to hyperinsulinemia [88–90]. Adiposity may increase CRC risk through insulin resistance, altered insulin-like growth factor signaling, dysregulated adiponectin, and gut microbiome [62,76,91]. Physical activity may lower CRC risk by improving insulin regulation, reducing inflammation/growth factors, accelerating gastrointestinal transit, or enhancing amino acid metabolism [63,92,93].

Strengths and limitations

Strengths of this review include prospective studies (median 12.3-y follow-up), examining dietary-lifestyle patterns on CRC risk and mortality within the CUP Global framework, presenting evidence on adiposity, physical activity, diet, alcohol, smoking, and sleep. No publication bias was detected for a priori patterns evaluated in $\geq$10 studies. Subgroup analyses explored potential effect modifications where sufficient studies existed. Most studies used validated food frequency questionnaires for diet and cancer registries or medical records for CRC diagnosis. Evidence was evaluated using standardized CUP Global grading criteria.

Limitations include the infeasibility of conducting a meta-analysis because of scoring inconsistencies and heterogeneity in pattern measurement. Approximately 68% of studies on a priori patterns used pre-established cut-off points, whereas some used percentiles, limiting comparability. Most studies used categorical exposures, hindering dose–response analyses. Subgroup/sensitivity analyses for a posteriori and hybrid patterns were limited by insufficient studies. Some studies lacked adjustment for total energy intake or confounders (for example, prior endoscopic screening), possibly altering association magnitudes or directions. Furthermore, baseline-only data may have diluted associations, and recall-based methods could introduce measurement errors. However, prospective designs likely led to non-differential misclassification, attenuating associations. Finally, the generalizability of findings is limited by the under-representation of younger, racially/ethnically diverse populations, including Black or African descent and non-Western backgrounds. Acknowledging these limitations, evidence was graded conservatively.

Future research should prioritize well-designed prospective cohort studies with consistent score definitions, repeated exposure/confounder assessments, and validated scores. Dose–response analyses are needed to explore associations, including increments and plateaus. Subgroup analysis can uncover heterogeneity. Incorporating emerging factors (for example, smoking and sleep) into scores would improve CRC risk assessment. Although RCTs are challenging, alternative approaches, including trial emulation and pooled cohort analyses, could strengthen causal evidence. To ensure equitable dietary-lifestyle recommendations, studies should include diverse populations, younger age groups, and life-stage-specific behaviors, whereas also exploring biological mechanisms.

Conclusions

Approximately a quarter of studies on healthy a priori dietary-lifestyle patterns showed strong inverse associations with CRC risk (RRs: 0.25–0.50), and nearly half showed moderate associations (RRs: 0.51–0.80). WCRF/AICR recommendations for lower CRC risk were graded "strong—probable," whereas ACS and HLI guidelines were "limited—suggestive" because of confounding concerns. These patterns emphasize healthy body weight, diet, limited red/processed meats, physical activity, and avoiding tobacco and alcohol. The hyperinsulinemic ELIH pattern showed "strong—probable" evidence for increased CRC risk. For cancer subsites, only the WCRF/AICR recommendations showed "strong—probable" evidence for lower

colon cancer risk. Evidence on CRC mortality remains lacking. These findings can inform health professionals, policymakers, researchers, and other stakeholders in promoting CRC prevention dietary-lifestyle strategies. Future work includes WCRF and the CUP Global Expert Panel developing recommendations based on these conclusions.

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Author contributions

The authors' responsibilities were as follows – DHL, ELG: were among the coauthors to the development of the protocol for this work; KL, AHYC: did the literature search, study selections, data extraction and assessed risk of bias, synthesized and interpreted the data; DSMC: checked the data; GM, KKT: prepared the tool related to risk-of-bias assessment; AHYC, KL, DHL, ELG: wrote the draft of manuscript; MPW, SJL, HC, SK, KKT, DSMC, GM, YP: critically reviewed the manuscript; ELG: supervised the study; JK: was Chair of the CUP Global Panel; MPW: was Co-chair of the CUP Global Panel; MLB: was Chair of the CUP Global Expert Committee on cancer incidence; YP: Deputy Chair of the CUP Global Expert Committee on cancer incidence; SJL, JCS, EC, RC, LH: were CUP Global Expert Panel members (all members of the Expert Panel provided input into the judgments on the evidence and advised on the interpretation of the review, with the Expert Committee providing the preliminary evidence interpretation, the public representative (LC) did not contribute to the final decisions made by the Panel. HC was Head of the CUP Global Secretariat); and all authors: revised and approved the manuscript.

Conflict of interest

The authors declare no conflict of interests.

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Data availability

For this review, only publicly published data were used. All information on data sources and handling is described in Methods section and Supplementary material. Further details could be available from the corresponding author upon request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajcnut.2025.01.014.

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