The Influence of Ultra-Processed Food on Colorectal Cancer: A Systematic Review

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Abstract: Colorectal cancer (CRC) is a disease characterised by the development of malignant tumours in the colon or rectum; it is considered the most common cancer in women, and up to 50% of cases can be prevented with a healthy lifestyle. Nutritional habits are related to its appearance, and the current trend of an increased consumption of ultra-processed foods (UPFs) has led to a surge in the incidence of CRC in recent years. This systematic review aims to evaluate, based on scientific evidence, the role of UPF in the incidence of CRC. The PubMed, Scopus, CINAHL, and Web of Science databases were reviewed, and a total of 24 scientific articles were selected according to the inclusion and exclusion criteria of this review (studies from the past 5 years and observational studies in English). The conclusions of this study point to an association between UPF-based diets and the appearance of CRC, which is promoted by the harmful effects of the consumption of high levels of sugar, fat, red meat, and additives. These dietary habits, coupled with a sedentary lifestyle and obesity, further increase the incidence of CRC.

Keywords: colorectal cancer; colorectal neoplasms; diet; food; lifestyle; nutrition; prevention; ultra-processed food

1. Introduction

Lifestyle is an important issue, and the scientific community is concerned about its influence on the occurrence of cancer [1]. Cancer stands out as one of the most prevalent diseases worldwide, positioning itself as the second leading cause of death after cardiovascular disease [2]. Diet has been identified as a risk factor for this disease; epidemiological studies show that the consumption of whole grains, fibre, fruits, and vegetables is associated with a lower risk of cancer [3–6].

The morbidity of cancer continues to grow worldwide, and among its forms, colorectal cancer (CRC) ranks third in prevalence within the disease according to data from the U.S. National Cancer Institute [3]. CRC is characterised by the appearance of malignant lesions in the epithelium of the intestinal mucosa, ranking as the second most common cancer in women and the third in men worldwide [4–6]. It is estimated that by 2030, the CRC rates will increase by 124.4% and 90%, respectively, in the population aged 20 to 34 years, reaching high prevalence [3,5].
The main risk factors for CRC include dietary habits, obesity, and lifestyle, among others [4–7]. Previous studies argue that dietary modifications can prevent 30 to 50% of CRC if fibre, grains, fruits, and vegetables are consumed [2,4,6]. Due to fast-paced lifestyles being common, novel dietary patterns have been adopted that favour the consumption of ultra-processed foods (UPFs). This is attributed to their ease of acquisition, consumption, and reduced cost compared to a Mediterranean diet. The consumption of UPFs is considered proportional to the level of development of a country [1,2,4].

These types of food exhibit low nutritional quality, a high glycaemic load, and insufficient fibre and micronutrients, predisposing people to an increased risk of CRC. In addition, there is an association between colorectal tumours and chronic inflammation [2,4,6,8–10]. Specific diet patterns can increase chronic inflammation by altering the microbiota of the body, thereby promoting the onset of tumours and precancerous lesions. Ultra-processed foods induce dysbiosis, a pro-inflammatory microbiota, where the intestinal permeability is affected, generating local chronic inflammation of the mucosa with the migration of lipopolysaccharides to the systemic level. This results in a state of chronic low inflammation, which some authors call “meta-inflammation”, that is, a state of chronic metabolic inflammation, which is behind many of today’s chronic diseases. To this, we must add data showing the epigenetic changes induced by metabolites of the microbiota that could be transmitted to the next generation [6–9].

The pathogenic effect of UPFs derives from their chemical compositions, since they contain substances such as acrylamide, polycyclic aromatic hydrocarbons, or heterocyclic amines (carcinogenic toxic products), which are generated due to the high temperatures reached during meat processing. The use of artificial sweeteners, such as sucralose, aspartame, saccharin, and others, modify the microbiota, as well as the use of colorants and emulsifiers, such as lecithin, carboxy methylcellulose, and guar gum, among others, which are widely used by the industry to improve UPFs’ organoleptic properties and appearance and extend their expiration dates [10–13].

Contaminants derived from their packaging should also be considered, such as bisphenol A (BPA), phthalates, microplastics, and nanoparticles, which can migrate into the foods, especially when they are displayed for sale for a long time [14].

On the other hand, their high sugar, refined oil, and saturated fat contents make them detrimental to people’s health, contrasting with their pleasant palatability that predisposes people to their consumption [7,8].

The WHO recommendations advise limiting the consumption of free sugars due to their associations with the onset of diabetes, obesity (a factor related to cancer spread), and hypertension [4,7]. Another category of foods that are harmful to people’s health includes trans fatty acids, which are increasingly present in industrial processing and found in high-fat foods that are unnecessary in the human diet. These are related to the development of cardiovascular diseases, diabetes, and cancer due to their pro-inflammatory properties and inhibitory effects on the metabolism of essential omega-3 and polyunsaturated omega-6 fatty acids [15,16].

Despite these concerns, few studies have evaluated the relationship between UPFs, such as sugar and others, with the onset of CRC [17]. This diet pattern modifies and disrupts the microbiota, which plays a crucial role in protecting individuals against pathogens [15,18]. The consumption of UPFs allows for the production of genotoxins and carcinogenic microbial metabolites, creating a pathological scenario that can favour the development of colorectal tumorigenesis (eubiosis) [8,10].

Although UPFs are considered nutritionally unfavourable, they have been approved for human consumption, and they have been the subject of toxicological studies and safety evaluations that have not been able to assess their possible long-term harmful effects regarding CRC [17]. Consequently, there is an emphasis on the need for studies that demonstrate the use and consumption of these foods in relation to CRC.

CRC is therefore a significant public health problem, and an awareness of its risk factors is necessary to reduce behaviours that increase the risk of this condition. Consequently, this
2. Methods

2.1. Search Strategy and Inclusion Criteria

A systematic literature review was conducted following the recommendations of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and the methodological framework of the Joanna Briggs Institute [19,20]. The review protocol was registered in PROSPERO under the following registration number: CRD42023482555 (available at https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023482555 (accessed on 24 November 2023).

The literature search was conducted, independently, by two researchers in four international health sciences databases. PubMed, SCOPUS, Web of Science (WOS), and CINAHL (Cumulative Index to Nursing and Allied Health Literature) were reviewed during October and November 2023. A comprehensive search of the grey literature was performed from specific repositories and Google Scholar to mitigate bias. In case of discrepancies among researchers regarding the inclusion of any article, a third researcher was consulted.

The search strategy was established using the Medical Subject Headings (MeSH) thesaurus, selecting the keywords: (“ultra-processed food” OR “junk food” OR “fast food” OR “unhealthy food”) AND (“colon” OR “colorectal” OR “bowel”) AND (“neoplasm” OR “cancer” OR “tumour” OR “carcinoma”).

Inclusion criteria were primary studies with observational, case–control, or cohort designs, in Spanish or English, with no temporal restrictions, which analysed the association between UPF consumption and the incidence of CRC in humans. No ethics approval committee was required for this study, as it is a systematic review that does not involve patients. Exclusion criteria were being systematic reviews, meta-analysis, clinical trials, or randomised clinical trials.

2.2. Data Selection and Extraction

The study selection was carried out independently by two researchers, and in case of disagreement, consultation was sought with a third member of the research team. Duplicates were removed using the Mendeley reference management tool through the “Check for duplicates” tab.

Initially, the titles and abstracts of the articles were reviewed, followed by a detailed evaluation of the full texts. In addition, a secondary search was conducted by reviewing the references of the selected studies. The agreement between the two researchers in assessing the suitability of the studies was quantified using the Kappa statistical test.

A double entry table was designed to collect information from each study, including: (1) the author’s name; (2) year of publication; (3) country of origin; (4) study design; (5) sample size; (6) type of UPF; (7) study objective; and (8) results obtained. Two reviewers, independently, conducted data collection and discussed their results with a third reviewer.

2.3. Risk of Bias

The ROB II (risk of bias in non-randomised studies of interventions) tool was used, categorising each type of risk into three levels: low, high, or unclear [16]. The rigorous use of ROB II allowed for a comprehensive and structured evaluation of possible biases in the included studies, addressing key aspects such as intervention allocation, outcome measurement, and participant selection.

3. Results

3.1. Results Obtained in the Selection of Articles

In the initial literature search, a total of 684 articles were identified, with non-additional documents included from other repositories. After removing 138 duplicate articles using the Zotero® reference manager tool, applying inclusion criteria and evaluating the titles and
abstracts of the articles, 660 articles were excluded because they did not meet the inclusion criteria. Finally, 24 studies were selected for systematic review analysis. The flow diagram (Figure 1) illustrates the review process. There was an excellent level of agreement between the researchers about the eligibility assessment of the articles (Kappa statistic = 0.91).

3.2. Bias Risk Assessment of the Selected Studies and Publication Bias

The risk of bias was assessed using ROB II and is represented in Figure 2 by a one-to-one summary plot. Almost all of the included studies exhibited a high risk of bias.

3.3. Descriptive Analysis of the Results Found

Table 1 shows the articles recovered in the presented search based on the different databases consulted. The years with the highest scientific production were 2020 (n = 8) and 2021 (n = 7). Regarding the epidemiological design of the studies, 2 studies followed a cross-sectional methodology, 12 were cohort studies, and 10 adopted a case-control design.
Figure 2. Bias assessment by a one-to-one summary plot [21–44].

3.3. Descriptive Analysis of the Results Found

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3.3.1. Sugar Consumption

Sugar is one of the main components and is significantly present in UPF, which favours hyperinsulinemia [44], chronic inflammation [26,27,38,44], and intestinal dysbiosis [26,33,38,44]. These components, according to the available scientific evidence, are mechanisms linking the diet with the CRC [23,44].

As a result, sugar intake is associated with an increased risk of CRC. Added sugars, free sugars, and sucrose are significantly present in sugary drinks such as sodas and in dairy products and desserts [25]. In this regard, some studies went further than simply associating sugar consumption with cancer in general but focused on colorectal neoplasia, demonstrating how a diet high in foods of a high glycaemic index significantly increases the risk of developing this pathology [23,25,40].

The high consumption of this substance leads to an increase in postprandial glucose responses, stimulating the production of pro-oxidant molecules that induce DNA damage, thus increasing the risk of tumours. This excessive intake can also generate advanced endogenous glycation products, which are highly reactive metabolites that trigger cytokine secretion and increased markers of oxidative stress production. Furthermore, refined sugars also result in a higher concentration of inflammatory markers (C-reactive protein) [25,31,43].
Table 1. Selected articles that met the inclusion and exclusion criteria of the study.

<table>
<thead>
<tr>
<th>Authors (Year) Country</th>
<th>Objective</th>
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<tbody>
<tr>
<td>Alessa et al. [21] 2023 Saudi Arabia</td>
<td>Assess the knowledge of the general population in Saudi Arabia about the relationship between UPF and CRC.</td>
<td>Cross-sectional study N = 802</td>
<td>Survey on sociodemographic, knowledge of UPF, and consumption rate</td>
<td>The study showed that a significant portion of the subjects ate UPF regularly and only a few were aware of its link with CRC. This highlights the need for greater knowledge of the fundamentals of UPF and its impact on health.</td>
<td>UC</td>
</tr>
<tr>
<td>Bradbury et al. [22] 2020 United Kingdom</td>
<td>To systematically examine the associations of CRC risk with food and food group intake.</td>
<td>Prospective cohort study N = 475,581</td>
<td>-FFQ Online dietary assessment 24 h</td>
<td>Consumption of processed and red meat at an average level of 76 g/day, which meets the current UK government recommendation (90 g/day), was associated with an increased risk of CRC. Alcohol was also associated with an increased risk of CRC.</td>
<td>AC</td>
</tr>
<tr>
<td>Chang et al. [23] 2021 Canada</td>
<td>Investigate the associations between various medical, lifestyle, and dietary factors and the risk of early-onset CRC.</td>
<td>Population-based case-control study N = 782</td>
<td>-Self-administered questionnaire on possible risk factors -Questionnaire on strenuous or moderate physical activities</td>
<td>Modifiable factors, particularly sedentary behaviour and an unhealthy diet, including the consumption of sugary beverages, may be associated with the risk of CRC.</td>
<td>SC, RPM, AC</td>
</tr>
<tr>
<td>Castelló et al. [24] 2018 Spain</td>
<td>To evaluate whether the associations found between three previously identified dietary patterns with breast, prostate, and gastric cancer are also observed for CRC.</td>
<td>Multicase-control study N = 5138</td>
<td>-Questionnaire on sociodemographic factors, lifestyle, and medical history -FFQ</td>
<td>No effect of the Prudent pattern on the risk of CRC was observed, but high adherence to the Western diet pattern was associated with an increased risk of CRC for men and women.</td>
<td>RPM</td>
</tr>
<tr>
<td>Debras et al. [25] 2020 France</td>
<td>To study the associations between total and added sugar intake and cancer risk, taking into account the types and sources of sugar.</td>
<td>Prospective cohort study N = 101,279</td>
<td>-Repeated and validated 24 h dietary records -Questionnaires on demographic, socioeconomic, and lifestyle characteristics</td>
<td>Sugars can represent a modifiable risk factor for CRC, contributing to the current debate on the implementation of sugar taxes, marketing regulation, and other sugar-related policies.</td>
<td>SC</td>
</tr>
<tr>
<td>The Kinany et al. [26] 2022 Morocco</td>
<td>Investigate the association between the consumption of foods and beverages of different processing categories and the risk of CRC among Moroccan adults.</td>
<td>Case-control study N = 2906</td>
<td>-FFQ -NOVA classification</td>
<td>The high consumption of UPF was significantly inverse, while the high consumption of processed foods was significantly positive in the association with the risk of CRC.</td>
<td>SC, RPM, FC, OF</td>
</tr>
<tr>
<td>The Kinany et al. [27] 2019 Morocco</td>
<td>To investigate the associations between adherence to WCRF/AICR cancer prevention recommendations and CRC risk in Morocco.</td>
<td>Population-based case-control study N = 3302</td>
<td>-FFQ -Physical activity questionnaire and anthropometric measurements</td>
<td>Compared to those with the lowest compliance score, those in the highest WCRF/AICR score category had a statistically significant reduced risk of CRC.</td>
<td>SC, OF</td>
</tr>
<tr>
<td>Fiolet et al. [28] 2018 France</td>
<td>To evaluate the possible association between UPF consumption and cancer risk.</td>
<td>Prospective population-based cohort study N = 104,980</td>
<td>-Repeated 24 h dietary records -NOVA classification</td>
<td>A 10% increase in the proportion of UPF in the diet was associated with a significant increase of more than 10% in the risk of CRC.</td>
<td>SC, RPM</td>
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<tr>
<td>Fliss-Isakov et al. [29] 2020 Israel</td>
<td>To examine the association between high UPF intake and colorectal adenomas and to test the interaction with smoking.</td>
<td>Case-control study N = 652</td>
<td>-Colonoscopy -Interview of sociodemographic factors, lifestyle, and medical history -FFQ</td>
<td>The positive association between UPF intake and adenomas was stronger with advanced adenomas and may reflect a potential role of UPF in the progression of CRC.</td>
<td>UC</td>
</tr>
<tr>
<td>Hang et al. [30] 2023 United Kingdom</td>
<td>The association between ultra-processed food and the risk of CRC.</td>
<td>Prospective observational cohort study N = 142,052</td>
<td>-Gastrointestinal endoscopy -Biannual lifestyle and medical information questionnaires. -FFQ</td>
<td>Higher UPF consumption is associated with an increased risk of CRC precursors. UPF may be a modifiable goal for the early prevention of CRC.</td>
<td>UC</td>
</tr>
<tr>
<td>Hur et al. [31] 2021 USA (a)</td>
<td>To study the association between sugary drinks and early-onset CRC.</td>
<td>Prospective cohort study N = 116,429</td>
<td>-FFQ -4 dietary indices: the main diet quality score and three plant-based dietary indices -Indices; and two mechanism-based indices: the Empirical Dietary and Lifestyle Index for Hyperinsulinemia</td>
<td>Higher intake of SSB in adulthood and adolescence was associated with a higher risk of EO-CRC among women. Reducing SSB consumption among adolescents and young adults may serve as a potential strategy to alleviate the increasing burden of EO-CRC.</td>
<td>SC</td>
</tr>
<tr>
<td>Jafari et al. [32] 2022 Iran</td>
<td>Determine the association between the consumption of UPF and CRC.</td>
<td>Case-control study N = 213</td>
<td>-FFQ</td>
<td>High intake of UPF is associated with an increased risk of CRC. Furthermore, among eight UPF categories, consumption of processed meat, fast foods, and non-dairy beverages was significantly higher in those who consumed a higher amount of UPF.</td>
<td>UC</td>
</tr>
<tr>
<td>Kunnavutthivanich et al. [33] 2020 Thailand</td>
<td>Explore the association between eating patterns and disease recurrence among Thai CRC patients.</td>
<td>Retrospective case-control study N = 225</td>
<td>-FFQ -GPAQ Version 2 Physical Activity Questionnaire</td>
<td>Among CRC patients with Thai diet lifestyles, there was no association between meat/wheat, fast food/processed fruit, or vegetarian diet patterns and CRC recurrence.</td>
<td>SC, FC</td>
</tr>
<tr>
<td>Mehrzad et al. [34] 2020 Iran</td>
<td>Investigate the independent and combined effects of some selected risk factors and the Arg399Gln XRCC1 polymorphism on CRC.</td>
<td>Case-control study N = 240</td>
<td>-Blood sample -FFQ</td>
<td>Gastrointestinal disorders, family history of cancer, BMI, and fast food consumption were significantly higher in cases than in controls.</td>
<td>RPM, AC, FC</td>
</tr>
<tr>
<td>Metha et al. [35] 2017 USA</td>
<td>To test the hypothesis that the associations of prudent diets and Western diets with the risk of CRC may differ depending on the presence of F nucleatum in tumour tissue.</td>
<td>Prospective cohort study N = 173,229</td>
<td>-FFQ</td>
<td>Diets rich in whole grains and dietary fibre are associated with a lower risk of F nucleatum-positive CRC, but not F nucleatum-negative cancer, which supports a potential role for the gut microbiota in mediating the association between diet and CRC.</td>
<td>RPM, OF</td>
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<tr>
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<tr>
<td>Nguyen et al. [36] 2021 USA</td>
<td>Relate the microbial metabolism of dietary sulphur to the incidence of CRC.</td>
<td>Prospective cohort study N = 59,013</td>
<td>-Lower endoscopy &lt;br&gt;-FFQ &lt;br&gt;Evaluation of dietary intake during adolescence</td>
<td>The findings support the role of dietary interactions with sulphur-metabolising gut bacteria in early-onset colorectal carcinogenesis, possibly beginning in adolescence.</td>
<td>OF, RPM</td>
</tr>
<tr>
<td>Romaguera et al. [37] 2021 Spain</td>
<td>To study whether the consumption of UPF and beverages is associated with breast, CRC, and prostate cancer.</td>
<td>Multicentre population-based case-control study N = 7834</td>
<td>-Multi case-control Spain &lt;br&gt;-FFQ &lt;br&gt;-NEW classification</td>
<td>An association was found between the consumption of UPF and beverages and an increased risk of CRC.</td>
<td>UC, SC</td>
</tr>
<tr>
<td>Schaberg et al. [38] 2020 USA</td>
<td>Characterisation of demographic and geographic differences in health beliefs and dietary habits related to the risk of CRC in adults in the United States.</td>
<td>Prospective observational study N = 838</td>
<td>-Survey of 12 questions on the HBM Likert scale &lt;br&gt;-DHQII &lt;br&gt;-MMQ &lt;br&gt;-Demographic and anthropometric information questionnaire</td>
<td>The health beliefs about the risk of coronary heart disease are influenced by the individual’s age and eating habits. Furthermore, regional differences in GLV consumption indicate opportunities for health messages focused on risk reduction.</td>
<td>SC, RPM, OF</td>
</tr>
<tr>
<td>Seyyedsalehi et al. [39] 2022 Iran</td>
<td>Explore the association between dietary trans fatty acid (TFA) intake and the risk of CRC.</td>
<td>Multicentre case-control study N = 4071</td>
<td>Personal interviews about lifestyle, dietary intake, education, smoking, opium use, socioeconomic status, physical activity, medical history, and NSAID use</td>
<td>Industrial TFAs, such as semisolid/solid hydrogenated oils, can increase the risk of CRC, especially colon and proximal colon cancer. On the contrary, ruminant TFAs do not appear to be associated with CRC.</td>
<td>UC, FC</td>
</tr>
<tr>
<td>Tayyem et al. [40] 2017 Jordan</td>
<td>To evaluate possible associations between the consumption of different fast foods and beverages and the risk of CRC in a Jordanian population.</td>
<td>Retrospective case-control study N = 501</td>
<td>-Sociodemographic questionnaires, diet history, anthropometric measurements, and physical activity metres &lt;br&gt;-FFQ</td>
<td>Consumption of some types of fast food, especially falafel, was associated with an increased risk of developing CRC. An elevated risk for potato chips and corn chips was found.</td>
<td>SC, FC</td>
</tr>
<tr>
<td>Wang et al. [41] 2021 USA</td>
<td>To develop a dietary score that correlates with intestinal bacteria that metabolise sulphur and examine their association with the risk of CRC.</td>
<td>Prospective cohort study N = 214,797</td>
<td>-Stool samples from consecutive bowel movements 1 to 3 days apart &lt;br&gt;Questionnaires on sample collection, lifestyle, and food frequency</td>
<td>Adherence to the microbial sulphur diet was associated with an increased risk of CRC, suggesting the potential of using dietary modification as a strategy for reducing risk in CRC.</td>
<td>RPM, OF</td>
</tr>
<tr>
<td>Xingcun Liu. [42] 2020 China</td>
<td>Analyse the relationship between factors related to dietary and environmental exposure and the incidence of CRC.</td>
<td>Case-control study N = 160</td>
<td>-Patients with CRC received treatments such as surgery or chemotherapy with XELOX &lt;br&gt;-CPSS of 14 items</td>
<td>The incidence of CRC was closely related to eating habits, environmental exposure, and psychological factors. Unhealthy eating habits, poor living environments, history of smoking and drinking, and excessive psychological pressure will increase the risk of CRC.</td>
<td>FC, AC, OF</td>
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### Table 1. Cont.

<table>
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<tr>
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<tr>
<td>Yantiss et al. [43] 2021 Canada</td>
<td>To examine associations between sugary drinks and the risk of breast, endometrial, ovarian, and/or CRC among women in the Canadian Diet, Lifestyle, and Health Study.</td>
<td>Cohort studies N = 73,909</td>
<td>-FFQ -Questionnaire on sociodemographic issues, personal medical history, physical activity, height and weight, and hormone replacement therapy</td>
<td>Relatively high SCB intake was associated with an increased risk of endometrial and ovarian cancer, but not breast or CRC.</td>
<td>SC</td>
<td></td>
</tr>
<tr>
<td>Zheng et al. [44] 2020 USA</td>
<td>Explore the role of poor dietary quality in the increasing incidence of CRC diagnosed before age 50.</td>
<td>Cohort study prospective N = 116,430</td>
<td>-FFQ every 4 years -Self-administered questionnaires on demographics, lifestyle factors, and medical diagnoses every 2 years</td>
<td>Poor diet quality was associated with an increased risk of early onset of high malignant distal and rectal adenomas. These findings provide preliminary but strong support for the role of diet in early-onset CRC.</td>
<td>SC, RPM, FC, OF</td>
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</table>

AC: alcohol consumption; CPSS: perceived psychological stress scale; DHQII: dietary health questionnaire II; FC: fat consumption; M: role of the microbiota; MMQ: meat module list; OF: other factors; RPM: red and/or processed meat; SC: sugar consumption; UC: association between different groups of UPF and CRC.

Regarding sugary drinks, a prospective cohort study involving a total of 116,429 nurses in the U.S. revealed that women who consumed two or more servings of sugary drinks per day had more than twice the risk of developing this pathology compared to those who consumed less than one serving per week, with a 16% increase in risk per serving per day. Furthermore, each increase in servings/day of sugary drinks during adolescence (13 to 18 years) was also reported to be associated with a 32% increase in the risk of developing early-onset CRC [31]. Sugary drinks contribute significantly to sugar intake in Western countries [25]. Other sweeteners, such as aspartame, have also been questioned. Although previous studies confirmed their safety, there are doubts about the possible long-term health consequences, as increased lymphomas and leukaemias have been reported in animal models [28].

3.3.2. Consumption of Red and/or Processed Meats

Various epidemiological studies have identified the consumption of processed and/or red meat as one of the risk factors for the development of CRC [23,24,26,34,44]. According to the WHO, it is the method of processing meat products that acts as a precursor to CRC. In this regard, the high-temperature processing of meat produces carcinogens such as N-nitroso or polycyclic aromatic hydrocarbons that are involved in the occurrence of malignant tumours, present in smoked, fried, or grilled meat (bacon, ham, hot dogs, etc.) [24].

However, another factor involved in the development of CRC is the method of preserving processed meat. Sodium nitrite, a preservative and colouring substance used in processed meats, could initiate or promote the development of preneoplastic lesions in the colon, as well as chronic intestinal inflammation [28,35,38]. In a study that followed 475,581 participants, those who consumed an average of 76 grammas of red and processed meat per day had a 20% higher risk of CRC compared to those who consumed 21 grammas in the same period [44].

On the contrary, Chang, Cotterchio, and Tinmouth (2021) did not obtain statistically significant results for the association between processed meat consumption and CRC. The study sample size could have been small, which could affect the results and consequently was lacking sufficient power to detect associations between these factors [23].
3.3.3. Fats Consumption

Regarding fat consumption, studies show a positive correlation between fat intake and increased proliferation of colon cells and associated risks [30,40]. In a clinical trial, a low-fat diet (20% of the energy from fat), a moderate-fat diet (30% of the energy from fat), and a high-fat diet (40% of the energy from fat) were compared. The result was an increase in intestinal flora associated with CRC in the high-fat diet group [44].

The type of fat ingested also plays a relevant role in the development of CRC. Fats known as healthy fats, such as polyunsaturated omega-3 fatty acids (PUFA), including alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), can act as protective agents against CRC due to their anti-inflammatory effect. EPA and DHA intake was inversely associated with an 11% and 12% lower risk of developing this pathology, respectively [44].

In contrast, saturated fatty acids were associated with tumorigenesis, and VLDL cholesterol, LDL cholesterol, triglycerides, and total cholesterol were positively correlated with the frequency of colon adenomas [38]. Furthermore, a positive association was found between industrial trans fatty acids (iTFA) and CRC, as they can play a mutagenic role, although meat trans fatty acids appear not to have an influence [26,33].

3.3.4. Alcohol Consumption

A study investigating the relationship between alcohol consumption and CRC showed that excessive alcohol consumption can increase the risk of developing it [42]. The data obtained in this study are consistent with those of other researchers such as Chang et al. or Xingcun et al. [23,42]. In the prospective cohort study conducted by Bradbury, Murphy, and Key (2020), each increase of 10 g/day in alcohol intake (equivalent to approximately half a pint of beer with 4.5% alcohol) was associated with an 8% increase in the risk of developing CRC [16].

Consumption of this substance diminishes the protection of the intestinal mucosa and alters the immune system. When ethanol reaches the intestine, it is converted into acetaldehyde, damaging cells. Additionally, it stimulates the secretion and synthesis of highly reactive oxygen species, damaging DNA and altering its methylation. This compound can also promote tumour growth through angiogenesis and immunosuppression, reducing the therapeutic effect of chemotherapy drugs. However, Mehrzad et al. (2020) did not find a statistically significant relationship between alcohol consumption and the risk of CRC, although the sample size was relatively small, so the results may not be very precise [34].

3.3.5. Other Related Factors

Regarding the impact of UPF on the microbiota and inflammation, additives such as saccharin and maltodextrin, commonly used in UPF, interact with the microbiota, promoting chronic intestinal inflammation or increasing bacteria, as argued previously. Nguyen et al. (2021) concluded that an increase in the sulphur microbial diet is associated with a higher risk of early onset adenomas in the colon and rectum [36].

Obesity is another risk factor, as this health condition is influenced by the type of diet and the patterns of physical activity. Authors like Zheng et al. (2020) and Mehrzad et al. (2020) showed that the BMI of individuals with CRC before their illness was significantly higher than that of those who did not have the disease [34,44]. Higher levels of BMI and waist circumference in adulthood are positively associated with the risk of CRC [26,27,38,44]. The overall risk of cancer death is 1.5 to 1.6 times higher in men and women with a BMI > 40 kg/m² [42]. Furthermore, a correlation has been observed between a country’s development and the risk of CRC, the consumption of a fibre-rich diet, or age [35,36].

4. Discussion

This systematic review aims to identify the scientific literature to analyse scientific evidence on the rapid and alarming growth of CRC in the population, significantly affecting
the younger demographic. The objective is to examine current scientific evidence on this serious disease, particularly in connection with the consumption of UPF.

As argued in the literature and supported by the meta-analysis by Godos et al. (2016), the diet content can potentially exert both protective and adverse effects on cancer risk. Fruit and vegetable-based diets are deemed healthy due to their fibre content, antioxidant compounds, and healthy fatty acids, including monounsaturated and polyunsaturated fatty acids. On the contrary, UPF-based diets, including alcoholic beverages, trans fatty acids, alcohol, and refined carbohydrates, are associated with an increased risk of digestive tract cancer [17].

A detailed analysis of the inclusion of UPF in dietary habits, as advocated by various studies, suggests a direct correlation between its regular consumption and the level of development of a country. This type of diet, coupled with sedentary behaviour and obesity, further increases the risk of this disease. This is justified by the high content of sugars, alcohols, and fats in UPF, which, when associated with obesity, increases risk. Adults in higher percentiles have a 29% higher likelihood of developing CRC, especially distal colon cancer [21].

UPFs are classified on a scale (NOVA) from group I to group IV based on the degree of processing they undergo. The Kinany et al. (2022) found that less processed UPFs (NOVA 1) play a less harmful role in the development of CRC than more processed ones (NOVA 4), increasing the risk of this pathology. These findings are reinforced by other studies linking UPF consumption with the appearance of this type of cancer [23,26–28,38,44,45].

Numerous investigations indicate that UPFs have higher levels of total fat, saturated fat, sugar, added alcohol, salt, additives, and toxic substances generated during processing. Additionally, they alter the protective microbiota, have a lower fibre density, and contain fewer vitamins that could provide protection. The low intake of components such as fibre or folate present in these foods may be more relevant to the development of CRC than other characteristics related to the processing of the diet [37]. For example, fried foods contribute to the development of CRC due to the accumulation of generated polycyclic aromatic hydrocarbons [30]. This effect is further exacerbated by typical packaging with plastic and bisphenol, increasing the carcinogenic impact [29,30,32,46,47].

This information contrasts with a cohort study conducted in France between 2009 and 2017, which found no significant relationship between UPF consumption and CRC risk. This discrepancy in the results could be attributed to the relatively short duration of the study to observe the development of CRC, as indicated by a prospective study conducted by Jafari et al. (2022). According to evidence from the meta-analysis by Morze et al. (2022), the Mediterranean diet, characterised by a high consumption of fruits, vegetables, and whole grains and a low consumption of red and processed meat, is correlated with a lower risk of cancer mortality in the general population [48]. Authors such as Castro et al. (2017), analysing 100 studies on risk factors for different histological types of gastrointestinal cancer, suggest that a diet high in fruits, vegetables, and unprocessed foods appears to reduce the risk of cancer [49].

Regarding sugar consumption, evidence from a published meta-analysis suggests that chronic inflammation can regulate carcinogenesis at various levels of tumour initiation, proliferation, and progression. This is manifested through accelerated cell proliferation, evasion of apoptosis, enhanced angiogenesis, and metastasis, as indicated by Michels et al. (2021) [50]. These findings align with those of various studies included in this systematic review.

In terms of fat consumption, as mentioned above, there is a positive correlation between fat consumption and the increased proliferation of colon cells and associated risks [34,46,51,52], specifically due to the consumption of saturated fatty acids (SFA). SFAs are related to tumorigenesis, VLDL and LDL cholesterol, triglycerides, and total cholesterol, all positively correlated with the frequency of adenomas in the colon [52]. However, a meta-analysis by Kim et al. (2019) did not show an effect of dietary fat or fatty acids on increased risk [49]. Two cohort studies in women also found no association between trans-fatty acid consumption and CRC. These authors argue that the published scientific evidence
is inconsistent with respect to the association between fat consumption and this disease, highlighting the need for further research to determine the influence of this nutrient [46,53].

Regarding the role of the microbiota and the consumption of UPF in CRC, diet is a determining factor in the integrity of the microbiome. It is suggested, as argued by Trakman et al. (2021), that the diet in the early years of life substantially influences the adult’s risk of health or disease. For example, exposure to UPF in childhood or adolescence can increase the risk of developing later inflammatory bowel disease or CRC [16,46]. Other authors, such as Viennois et al. (2017), demonstrated that emulsifiers (food additives used in numerous UPF to help mix substances that normally separate when combined) promote microbiota invasion and increase pro-inflammatory flagellin and lipopolysaccharide levels. This is associated with the creation of a pro-inflammatory environment, linked to imbalances in proliferation and apoptosis, resulting in exacerbated carcinogenesis [46,53].

However, despite the general trend in studies indicating a relationship between UPF consumption and CRC, supported by recent meta-analyses by Isaksen and Dankel (2023) and Largo et al. (2023) [35,54–56], other studies produce contradictory results. This is because there are other relevant factors that can significantly influence the acquisition of healthy habits. In this sense, in addition to UPF, several extrinsic factors can significantly influence the development of these lesions. The authors argue that obesity is a risk factor and that this situation is logically affected by the type of diet and physical activity. Several studies, including those by Zheng et al. (2020) and Mehrzad et al. (2020), showed that the BMI of CRC individuals before their illness was significantly higher than that of those without the disease [34,44].

This review has direct implications for clinical practice, highlighting greater awareness and education of the risks associated with the consumption of UPF and the development of CRC. Healthcare professionals should consider the integration of specific recommendations to reduce UPF consumption as part of CRC prevention strategies. Additionally, promoting dietary patterns rich in fruits, vegetables, and less processed foods may be crucial in reducing the risk of this disease. Open discussion and public awareness of potential links between diet, especially UPF consumption, and colorectal health could contribute to positive changes in eating habits and ultimately lead to a decrease in the incidence of CRC. It is crucial to encourage further research to better understand the underlying mechanisms and inform more specific intervention strategies in the clinical domain.

Finally, this systematic review has several associated limitations that need to be addressed, as they could influence and bias the findings. On the one hand, the diversity in the designs and methodological approaches of selected studies stands out, which could lead to result variability. Furthermore, the potential presence of publication bias could affect the validity of the results, generating a bias toward positive findings. The reliability of self-reported data on food intake, temporal and geographical variability, and dietary culture are other significant limitations. The heterogeneity of the results, the subjective assessment of the quality of the study, and the limitations of the tools used for this purpose also affect confidence in the results. These limitations underscore the need to interpret the results with caution and highlight key areas for future research that addresses identified gaps in the scientific literature, potentially through the development of a new updated meta-analysis.

Finally, and also as a prospective line of research, there is a need to assess possible differences in UPF consumption patterns and their relationship with CRC between men and women. Lin et al. highlight in their results that stratified analyses showed a positive relationship between the consumption of ultra-processed foods (UPFs) and an increased risk of colorectal cancer in men, but not in women [57]. The findings are somewhat consistent with a previous study on inflammation from ultra-processed foods, which suggests that men are more predisposed to the carcinogenic effects of the diet [58]. Possible explanations for such different sex patterns may involve the effect of sex hormones or genetics [59] or higher calcium intake (protective effect) by women [14]. However, one
must go beyond biological assessments and evaluate these differences from a biological and social perspective [60,61].

It would therefore be necessary to analyse this relationship from a gender perspective, assessing the consumption patterns of both men and women and the role played by differential gender socialisation. Similarly, future studies should assess the modulating role of sedentary behaviours in the relationship between CRC and UPF consumption.

5. Conclusions

The current scientific literature suggests that high consumption of UPF may entail an increased risk of developing CRC. This situation arises from an elevated sugar intake (resulting in hyperinsulinemia, dysbiosis, and predisposition to chronic inflammation), as well as the consumption of processed red meat, alcohol, and saturated fats. UPFs negatively impact the microbiota, and current scientific evidence suggests that alterations in the human intestinal microbiota are related to CRC. Individuals with this pathology exhibit a decrease in overall microbiota diversity and reduced levels of anti-inflammatory genera, coupled with an increase in pro-inflammatory genera. This imbalance leads to an increase in pathogenic bacteria and chronic intestinal inflammation, strongly associated with CRC.

Other factors such as higher BMI levels and a sedentary lifestyle can contribute to this disease by promoting cell proliferation, systemic inflammation due to hypertrophy of adipose tissue, and alterations in the immune system. Therefore, conducting new meta-analyses to analyse this relationship is essential.

Furthermore, it is identified that there is a need to develop healthy eating strategies and increase public awareness of the risk associated with UPF consumption with respect to CRC.

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Abbreviations

AC  Alcohol Consumption
ALA  Alphalinolenic Acid
BMI  Body Mass Index
BPA  Bisphenol A
CINAHL Cumulative Index to Nursing and Allied Health Literature
CPSS Perceived Psychological Stress Scale
CRC  Colorectal Cancer
DHA  Docosahexanoic Acid
DHQII Dietary Health Questionnaire II
DNA  Deoxyribonucleic Acid
EPA  Eicosapentaenoic Acid
FC  Fat Consumption
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