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LITERATURE REVIEW

Mediterranean Diet versus a Low-Carbohydrate Diet in Reducing Colorectal Cancer Risk

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Abstract

Background: A variety of foods have been studied in relation to colorectal cancer risk. There is research on certain foods that cause colon cancer or have a protective factor against it but there is limited research comparing diets. While the literature indicates a benefit to the Mediterranean diet in reducing the risk of colon cancer, studies on a low-carbohydrate diet, such as the Atkins or ketogenic diets, and the incidence of colorectal cancer are less common. Therefore, this study aims to compare the Mediterranean diet and a low-carbohydrate, high-fat diet in relation to colorectal cancer risk.

Methods: A PubMed literature search for relevant articles was conducted through August 2020 to identify potential links of the Mediterranean diet and low-carbohydrate, high-fat diet to colorectal cancer with preference being given to articles after 2015. Preference were given to studies that were systematic reviews, meta-analyses, randomized controlled trials, and cohort studies, but case control studies were accepted. The studies included had to be human studies that reported risk estimates and measures of variability (95% confidence intervals). Seventeen pertinent articles were retrieved and they served as the basis for this clinical review.

Results: There are no studies comparing Mediterranean and low-carbohydrate diets specifically. While specific diets are not compared, the foods and food groups that are key to both diets have been studied in relation to colon cancer risk. A Mediterranean diet focuses on fish, poultry, unsaturated fats, whole grains, fruits, vegetables, nuts, and legumes. A low-carbohydrate diet focuses on low-carbohydrate, high fat, and moderate protein with a variation in grams of carbohydrates consumed daily. Fish, red meats, poultry, eggs, oils, full-fat dairy, non-starchy vegetables, berries, nuts, and seeds are allowed while starchy vegetables and fruits, legumes, and whole grains are restricted.

Studies suggest that red meat can increase colorectal cancer risk. Fish may be a protective factor against CRC. There is no association between CRC and poultry. Whole grains, cereal fiber, and dairy products may decrease the risk. It is suggested that cruciferous vegetables may decrease CRC risk, but no consensus was obtained for fruits or fats. Studies suggest that the Mediterranean diet can decrease the risk of colon cancer.

Conclusion: Studies suggest that the Mediterranean diet reduces colorectal cancer risk. No studies on a low-carbohydrate diet and colorectal cancer are known. If a person is participating in a low-carbohydrate diet, they should be aware of which foods can increase risk of colon cancer and modify the diet to avoid these, specifically limiting the amount of red meat and finding other ways to receive a protein source. The two diets need to be directly compared to determine if the risk of colorectal cancer is more effectively reduced with the Mediterranean diet than a low-carbohydrate diet.

Keywords

Colorectal cancer, Colon cancer, Mediterranean, Reduced-carbohydrate, Low-carbohydrate, LCHF, Carbohydrate, Atkins, Ketogenic, Olive oil, Meat, Fish, Chicken, Red meat, Fat, Saturated, Unsaturated, Sugar, Whole grains, Dairy, Fruit, Vegetable, Nuts

Abbreviations

CRC: Colorectal Cancer; USPSTF: United States Preventative Services Task Force; MedD: Mediterranean Diet; LCHF: low-Carbohydrate High-Fat; RR: Relative Risk; CI: Confidence Interval; HR: Hazard Ratio; DII: Dietary Inflammatory Index; CRA: Colorectal Adenoma; CV: Cruciferous Vegetables; BMI: Body Mass Index; GI: Gastrointestinal

Introduction

Colorectal cancer (CRC) is a deadly disease that affects 4.7 million people a year with 1.8 million new diagnoses in 2018 [1]. In the United States, there were

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approximately 147,000 new cases in 2018, making it the third most common type of cancer [1]. It is estimated that in 2020 nine percent of new cancer cases will be colorectal [2]. While the overall rate of colorectal cancer is decreasing in the United States, the number of people less than fifty years of age being diagnosed is increasing by two percent per year [3].

Screening tools and guidelines have been implemented to detect colorectal cancers, ideally at early stages before metastasis occurs. The United States Preventative Services Task Force (USPSTF) recommends that colorectal cancer screening be performed between the ages of 50 and 75 when there are no increased risk factors [4]. The different tests for screening include colonoscopy, flexible sigmoidoscopy, stool tests, and imaging, including computed tomographic colonography [4].

While the USPSTF recommends screening beginning at age 50, the American Cancer Society recently updated their recommendations for colon cancer screening to start in adults at age 45 with a high-sensitivity stool-based test or visual examination [5]. This updated recommendation was implemented because of the incidence rates of colon cancer increasing in younger populations and studies showing a benefit to start screening at an earlier age [5].

If there are risk factors, such as familial or hereditary syndromes, or inflammatory bowel diseases, the screening recommendations are modified. There are, however, other risk factors that do not affect screening recommendations; they include obesity, diabetes mellitus, smoking, alcohol use, and red meat consumption [6-8]. The incidence of colorectal cancer is increasing in adults aged forty to forty-nine. They are being symptomatically diagnosed at later stages, which show a true increase in risk and not just earlier detection [9]. With this increased incidence, health care providers need to educate patients on risk factors, as well as protective factors to help reduce this number. Many of these factors revolve around an appropriate diet with proper education.

When patients schedule appointments for annual wellness visits, part of a clinician's job is to educate them on proper diet and exercise for overall health with specific suggestions and lifestyle modifications for chronic medical conditions. Patients try different diets to lose weight, maintain weight, and manage these chronic conditions. Some diets, although they may help with losing or maintaining weight, could potentially increase the risk of colorectal cancer. There is a variety of diets for people to choose from. Two diets ranked as "Best Weight-Loss Diets" are the Mediterranean and Atkins' diets [10]. The Mediterranean diet (MedD) focuses on complex carbohydrates and healthy fats with few red meats, sugars, and saturated fats while the Atkins diet focuses on low carbohydrate, high fat (Table 1) [10-12].

The MedD consists of seafood and poultry with red meat in moderation, as well as nuts and legumes for a protein source [13]. Monounsaturated olive oil is the primary source of fat. Whole grains, including barley, oats, brown bread, and brown rice are included with this diet. Daily intake of fruits and vegetables are also important. This diet does not specify food items to eat or amount of calories to consume.

The average daily intake of macronutrients is 45% from carbohydrates, 35% from fats, and 15% from protein [14]. In a low-carbohydrate, high-fat (LCHF) diet, the amount of carbohydrates can vary. A very low-carbohydrate diet is less than ten percent of macronutrients coming from carbohydrates which equates to 20-50 grams per day [12]. A low-carbohydrate diet is less than 26% coming from carbohydrates which are less than 130

Table 1: Food groups included or excluded in the following diets: Mediterranean, Atkins, and Ketogenic.

		Low-carbohydrate, high-fat (LCHF)	
	Mediterranean	**Atkins**	**Ketogenic**
Seafood	Allowed	Allowed	Allowed
Poultry	Allowed	Allowed	Allowed
Red Meat	In Moderation	Allowed	Allowed
Nuts	Allowed	Allowed	Allowed
Whole grains	Allowed	Restricted	Restricted
Sugars	Restricted	Restricted	Restricted
Legumes	Allowed	Restricted	Restricted
Starchy Vegetables	Allowed	Restricted	Restricted
Non-starchy Vegetables	Allowed	Allowed	Allowed
Starchy Fruits	Allowed	Restricted	Restricted
Non-starchy Fruits	Allowed	Allowed	Allowed
Low-fat Dairy	Allowed	Allowed	Allowed
High-fat Dairy	In Moderation	In Moderation	Allowed
Vegetable oil	Allowed	In Moderation	Allowed

grams per day [12]. In a standard ketogenic diet, the macronutrients are broken down so that five percent is carbohydrates, 75% is fat, and 20% is protein [15]. The standard Atkins' diet has a carbohydrate restriction in the first two weeks to twenty grams per day which then increases to fifty grams [16]. The ideal percentages in a LCHF diet are 5-10% carbohydrates, 20-30% protein, and 60-70% fat [16].

In an LCHF diet, fish, red meats, poultry, eggs, oils, full-fat dairy, non-starchy vegetables, berries, nuts, and seeds are allowed [15]. Sugars are restricted, as well as starchy vegetables and fruits, legumes, whole grains, and alcoholic beverages (Table 1) [15]. In the Atkins' diet, high-fat dairy and oils are recommended in moderation (Table 1) [16].

Clinicians need to be knowledgeable about what foods and percentages of macronutrients make up each diet. With evidence of certain foods being risk factors for, and some being protective factors against colorectal cancer, the clinician needs to be educated in dietary recommendations for patients regarding chronic medical conditions as well as risks of malignancies. This clinical review article explores the effectiveness of the Mediterranean diet versus a low-carbohydrate diet in the reduction of colorectal cancer.

Methods

An extensive PubMed literature search was conducted through September 2020 using a combination of MeSH terms, Title/Abstract, and Text Word with preference being given to articles after 2014. The search terms were selected based on colorectal cancer, Mediterranean diet, and a low-carbohydrate, high-fat diet. The following combination of search terms were used and combined with Boolean operator AND/OR: "colorectal cancer", "colon cancer", "Mediterranean", "reduced-carbohydrate", "low-carbohydrate", "LCHF", "Atkins", "ketogenic", "olive oil", "meat", "fish", "chicken", "red meat", "fat", "saturated", "unsaturated", "sugar", whole grains", "dairy", "fruit", "vegetable", and "nut".

No language restrictions were imposed. Preference were given to studies that were systematic reviews, meta-analyses, randomized controlled trials, and cohort studies, but case control studies were accepted. Articles that described the impact of certain diets or food groups on colorectal cancer were screened first according to titles and abstracts; the full-text articles were then assessed for eligibility. The reference lists of the selected articles were screened for further relevant studies.

The review inclusion criteria were: (1) Human studies and (2) Report risk estimates and measures of variability (95% confidence intervals). The exclusion criteria included: (1) Review papers, editorials, or book chapters, (2) Animal studies, and (3) Studies that did not have data on specific food groups from each diet.

This review only included foods that were present in either a MedD or LCHF diet since there was no research specifically comparing an LCHF diet with colorectal cancer.

The Mediterranean diet was defined as a diet that allowed fish and poultry, nuts, legumes, all fruits and vegetables, whole grains, monounsaturated fats (olive oil) with avoidance of sugars and saturated fats with red meat in moderation.

A low-carbohydrate, high-fat diet was defined as allowing fish, poultry, red meat, eggs, full-fat dairy, non-starchy veggies and fruits, berries, nuts, seeds, and high-fat oils with avoidance of sugars, starchy vegetables, starchy fruits, legumes, and whole grains.

Results

Seventeen pertinent articles were retrieved and served as the basis for this clinical review (Table 2 and Table 3).

Mediterranean diet

Overall, the studies targeting the Mediterranean diet showed a significant reduction in colorectal cancer risk [17,18]. High adherence was shown to significantly reduced CRC risk [17]. One study reported an 18% reduced risk in women with strict adherence [18].

LCHF diet

No studies evaluating a low-carbohydrate, high-fat diet and colorectal cancer association were identified.

Red meats

Seven studies, which consisted of cohort studies, systematic reviews, and meta-analyses, were used to evaluate red meat association with colorectal cancer. Three of the studies showed a positive association with colorectal cancer, two had no significant associations, and two had mixed results depending on sex and/or tumor location [17-23]. In the studies, red meat was defined as unprocessed beef and pork intake. Some studies differentiated the two while others categorized the study as red meat overall.

Studies varied in the amount of daily red meat consumption with multiple studies showing an increase in CRC risk with greater than 100 grams per day [19-21]. One hundred grams per day of red meat was weakly associated with CRC and significantly associated with colon cancer [19]. This positive association was duplicated in a meta-analysis of 28 studies of red meat where there was an increased risk of CRC with red meat [20].

One study compared low intake of red meat with never or less than 27 grams per day and high intake of 3-4 times per week or more than 54 grams per day [22]. This study showed that those with a high intake of red and processed meat had a 10% increased colorectal

Table 2: Overview of study characteristics and main findings.

First author (Year)	Study Design	# studies	# participants	# CRC cases	Main findings with HR, OR, RR, 95% CI, p value
Barrubes (2019)	Systematic review and meta-analysis of cohort and case-control studies	29	1,396,167	22,654	Total dairy per 1 serving increment of 200 g had an inverse association with CRC (RR = 0.92, 95% CI 0.88, 0.96, p < 0.001) Total milk per 1 serving increment of 200 g had an inverse association with CRC (RR = 0.90, 95% CI 0.86, 0.99, p < 0.001) Total cheese per 1 serving increment of 30 g had an inverse association with CRC (RR = 0.93, 95% CI 0.88, 0.99, p = 0.006) There was no significant association between CRC and low-fat dairy or whole milk
Ben [25]	Meta-analysis of observational studies	22	*Not provided*	11,696 CRA cases	There was no association with fruits and vegetables combined at 100 g/day or vegetables at 100 g/day with colorectal adenoma (CRA) which is the precursor to CRC Significant reduction in CRA risk with fruits at 100 g/day (RR = 0.94, 95% CI 0.92, 0.97)
Bernstein (2015) [21]	Cohort	2	3,452,754 person-years	2731	Processed red meat consumption was positively associated with CRC risk, specifically with distal colon cancer at 30 and 50 g/day increase (HR 1.36, 95% CI 1.09-1.69, p = 0.006) Unprocessed red meat was inversely associated with distal colon cancer at 1 serving per day of 100 and 120 gram increase (HR 0.75, 95% CI 0.68-0.82, p < 0.001)
Bradbury [26]	Prospective cohort study	27	~470,000	2819 in fruit and vegetable intake 4517 in fiber intake	Total fiber showed significant inverse associations with colorectal cancer risk (RR = 0.83, 95% CI 0.72, 0.96, p = 0.013 but when looking at different fiber types, only cereal fiber was significant (RR = 0.87, 95% CI 0.77, 0.99, p = 0.003), not fruit and vegetable fiber No statistical significance when fruit and vegetables were combined (RR = 0.97, 95% CI 0.93, 1.01) at 100 g/day increase in intake
Carr [22]	Systematic review and meta-analysis of prospective studies	19	Ranging from 639 to 492,186	15,183	Beef had an increased CRC risk (RR = 1.11, 95% CI = 1.01, 1.22) Pork had no CRC association (RR = 1.07, 95% CI = 0.90, 1.27) Poultry had no CRC association (RR = 0.96, 95% CI 0.88, 1.04) Red and processed meat at a high intake (3-4x per week or > 54 g/day) had a 10% increased CRC risk

Jones [18]	Cohort	1	32,154	465	Women with high adherence to a MedD diet showed an 18% reduced risk (HR = 0.88, 95% CI 0.78, 0.99). Red meat and poultry had no significant association at low, medium, or high intake
Kim [33]	Systematic review and meta-analysis of original and prospective cohort studies	18	*Not provided*	*Not provided*	There was no significant association between CRC risk and total fat (RR = 1.00, 95%CI 0.90, 1.12), saturated fat (RR = 0.97, 95%CI 0.86, 1.10), monounsaturated fat (RR = 1.08, 95%CI 0.92, 1.26) and polyunsaturated fats (RR = 0.99, 95%CI 0.93, 1.04)
Ma [31]	Meta-analysis of original research and prospective cohort studies	11	~ 1,450,500	9,618	An inverse association for dietary fiber was demonstrated in high vs. low fiber intake in proximal colon cancers with a lower risk of 14% (RR = 0.86, 95%CI 0.78, 0.95, p = 0.664) Distal colon cancer risk was 21% lower in the high vs. low fiber intake (RR = 0.79, 95%CI 0.71, 0.87, p = 0.163)
Reynolds [30]	Systematic review and meta-analysis of RCTs and prospective studies	10	8.8 million person-years	11,245	Total fiber showed an inverse association with CRC risk for every 8g more of fiber consumed per day (RR = 0.92, 95%CI 0.89, 0.95) with the greatest benefit at 25-29 g/day Whole grains had an inverse association with CRC risk (RR = 0.97, 95%CI 0.95, 0.99) for every 15 g more per day
Schwing-shackl [17]	Systematic review and meta-analysis of cohort and case-control studies	83 total studies 11 for CRC	2,130,753 in all studies	Cohort: 15,108	No significant associations with meats or fish Higher adherence to MedD diet showed an inverse association with colorectal cancer risk (RR = 0.82, 95% CI 0.75, 0.88)
Schwing-shackl (2018)	Systematic review and meta-analysis of prospective studies	86	*Not provided*	*Not specifically given-broken down by food group*	Increased risk of CRC with red meat at 100 g/d (RR = 1.12, 95% CI 1.06, 1.19) Trend for an inverse association for 100 g/day of fish (RR: 0.96, 95% CI 0.90, 1.01) Inverse association for whole grains for each 30 g/day (RR = 0.95, 95% CI 0.93, 0.97) , fruit at 100 g/d (RR 0.97, 95% CI 0.95, 0.99), and dairy at 200 g/d (RR 0.93, 95% CI 0.91, 0.94) Small inverse association in vegetables at 100 g/d (RR: 0.97, 95% CI 0.96, 0.98) No CRC association in nuts, legumes
Shivappa [28]	Meta-analysis of case-control and cohort studies	9	881,612	18,888	Higher scores in the dietary inflammatory index (DII) are associated with colorectal cancer High vs. low DII showed a 40% increase in CRC risk (RR = 1.40, 95% CI 1.26, 1.55, p < 0.001) There was an increased risk of CRC of 7% for each increase in 1 point in the DII score (RR = 1.07, 95% CI 1.04, 1.10, p < 0.00001)

Vieira [19]	Systematic review and meta-analysis of prospective studies	111	*Not provided*	Median number of 6662 Ranging from 729 to 31,551	100 g/day of red meat was significantly associated with CRC (RR = 1.12, 95% CI 1.00, 1.25) and colon cancer (RR 1.22, 95% CI 1.06, 1.39) 11% decreased CRC risk of 100 g/day of fish (RR = 0.89, 95% CI 0.80, 0.99) 90 g/day of whole grains reduced CRC risk (RR = 0.83, 95% CI 0.79, 0.89) 100g/day of vegetables decreased CRC risk (RR = 0.98, 95% CI 0.96-0.99) Higher dairy intake at 400g/day decreased CRC risk (RR = 0.87, 95% CI 0.83, 0.90) Higher milk intake at 200g/day decreased CRC risk (RR = 0.94, 95% CI 0.92-0.96) No association with CRC included: Poultry at 100 g/day, fruit intake, legumes at 50 g/day, and cheese
Vulcan [23]	Prospective cohort	1	27,931	728	High intake of beef was inversely associated with colon cancer (HR 0.60, 95% CI 0.44, 0.82, p = 0.0009). Beef increased the risk of rectal cancer in men (HR 1.28, 95% CI 1.02, 3.25, p = 0.028) Beef intake was inversely associated with CRC in women (HR 0.65, 95% CI 0.45 to 0.95, p 0.046) Pork increased the incidence of CRC (HR 1.39, 95% CI 1.09, 1.78, p = 0.023) Poultry had no CRC association Fish intake had an inverse association with rectal cancer (HR 0.59, 95% CI 0.38, 0.92, p = 0.025) Intake of red meat should not exceed 500 g/week The type of meat as well as sex and tumor location influence CRC associations
Wu [29]	Meta-analysis of case-control and cohort studies	35	1,295,063	24,275	Inverse association between CV and CRC risk (RR 0.82, 95% CI 0.75, 0.90) seen better in case-control and only borderline significance in cohort studies
Yu [24]	Meta-analysis of cohort studies	42	2,325,040	24,115 GI cancers	Fish consumption had a reduced risk of CRC (RR 0.93, 95% CI 0.87, 0.99, P < 0.01)
Zamora-Ros[27]	Prospective cohort study	1	477,312	4,517	No statistical significance in total flavonoid intake (HR 1.05, 95% CI 0.93, 1.18, p = 0.58) or flavonoid subclasses was observed with CRC risk

Table 3: Summary of findings for positive, negative, or no association in studies.

Mediterranean diet [17,18]		
	Schwingshackl [17]	High adherence significantly reduced CRC risk (RR = 0.82, 95% CI 0.75, 0.88)
	Jones [18]	18% reduced risk in women with strict adherence (HR = 0.88, 95% CI 0.78, 0.99)
LCHF		
	---	No studies were identified
Red meats [17-23]		
	Schwingshackl [17]	No significant association
	Jones [18]	No significant association
	Vieira [19]	100 g/d of red meat was weakly associated with CRC (RR = 1.12, 95% CI 1.00, 1.25) and significantly associated with colon cancer (RR 1.22, 95% CI 1.06, 1.39)
	Schwingshackl, et al. [20]	Increased risk of CRC with red meat (RR = 1.12, 95% CI 1.06, 1.19)
	Bernstein [21]	Processed red meat was positively associated with CRC risk (HR 1.36, 95% CI 1.09-1.69, p = 0.006) Unprocessed red meat was inversely associated with distal colon cancer (HR 0.75, 95% CI 0.68-0.82, p < 0.001)
	Carr [22]	Beef increased CRC risk (RR = 1.11, 95% CI = 1.01,1.22) while pork had no association (RR = 1.07, 95% CI = 0.90, 1.27).
	Vulcan [23]	Pork incidence increased the incidence of colorectal cancer (HR 1.39, 95% CI 1.09, 1.78, p = 0.023) and beef increased the risk of rectal cancer in men (HR 1.28, 95% CI 1.02, 3.25, p = 0.028) An inverse CRC risk was noted in women (HR 0.65, 95% CI 0.45, 0.95, p 0.046) and high intake of beef was inversely associated with colon cancer (HR 0.60, 95% CI 0.44, 0.82, p = 0.0009)
Poultry [18,19,22,23]		
	Jones [18]	No significant association
	Vieira [19]	No significant association
	Carr [22]	No association with CRC (RR = 0.96, 95% CI 0.88, 1.04) but an inverse association with rectal cancer (RR = 0.89, 95% CI 0.80, 0.98)
	Vulcan [23]	No significant association
Seafood [17,19,20,23,24]		
	Schwingshackl [17]	Inverse association and protective factor
	Vieira [19]	Decreased CRC risk by 11% with 100 g/day (RR = 0.89, 95% CI 0.80, 0.99).
	Schwingshackl, et al. [20]	Inverse association at 100 g/day (RR: 0.96, 95% CI 0.90, 1.01).
	Vulcan [23]	Inverse association with rectal cancer (HR 0.59, 95% CI 0.38, 0.92, p = 0.025)
	Xiao-Feng [24]	Reduced risk of CRC (RR 0.93, 95% CI 0.87, 0.99, P < 0.01)
Fruits [19,20,25-28]		
	Vieira [19]	No significant association
	Schwingshackl, et al. [20]	Inverse association (RR 0.97, 95% CI 0.95, 0.99)
	Ben [25]	Significant reduction in CRA risk at 100 g/day (RR = 0.94, 95% CI 0.92, 0.97)
	Bradbury [26]	No statistical association was found in combining fruit and vegetables at 100 g/day increase (RR = 0.97, 95% CI 0.93, 1.01)
	Zamora-Ros [27]	No statistical significance in total flavonoid intake (HR 1.05, 95% CI 0.93, 1.18, p = 0.58) or flavonoid subclasses
	Shivappa [28]	Comparing high vs. low DII showed a 40% increase in CRC risk (RR = 1.40, 95% CI 1.26, 1.55, p < 0.001)

Vegetables [19,20,25,26,29]		
	Vieira [19]	Inverse association with CRC risk (RR = 0.98, 95% CI 0.96-0.99)
	Schwingshackl, et al. [20]	Inverse association with CRC risk (RR: 0.97, 95% CI 0.96, 0.98).
	Ben [25]	No association with CRA
	Bradbury [26]	No statistical association when increasing fruit and vegetables 100 g/day (RR = 0.97, 95% CI 0.93, 1.01)
	Wu [29]	Inverse association between cruciferous vegetables and CRC risk (RR 0.82, 95% CI 0.75, 0.90)
Whole grains [19,20,30]		
	Vieira [19]	Decrease in CRC risk with 90 g/d (RR = 0.83, 95% CI 0.79, 0.89)
	Schwingshackl, et al. [20]	Decrease in CRC risk with 30 g/d (RR = 0.95, 95% CI 0.93, 0.97).
	Reynolds [30]	Association for every 15 g more per day (RR = 0.97, 95% CI 0.95, 0.99)
Fiber [26,28,30,31]		
	Bradbury [26]	Significant inverse associations with total fiber intake (RR = 0.83, 95% CI 0.72, 0.96, p = 0.013) and cereal fiber (RR = 0.87, 95% CI 0.77, 0.99, p = 0.003)
	Shivappa [28]	Each 1-point increase in the DII score led to an increased risk of CRC of 7% (RR = 1.07, 95% CI 1.04, 1.10, p < 0.00001).
	Reynolds [30]	Inverse association with total fiber for every 8g more per day (RR = 0.92, 95%CI 0.89, 0.95)
	Ma [31]	Inverse association in proximal colon cancer (RR = 0.86, 95%CI 0.78, 0.95) and distal colon cancer (RR = 0.79, 95%CI 0.71, 0.87)
Dairy [19,20,32]		
	Vieira [19]	Decreased CRC risk at 400 g/d (RR = 0.87, 95% CI 0.83, 0.90). Decreased CRC risk at milk intake of 200 g/day (RR = 0.94, 95% CI 0.92-0.96) No association with cheese intake
	Schwingshackl, et al. [20]	Inverse association at 200 g/d (RR 0.93, 95%CI 0.91, 0.94)
	Barrubés [32]	Inverse association at 200 g/d (RR = 0.92, 95% CI 0.88, 0.96, p < 0.001) Inverse association with milk intake at 200 g/day (RR = 0.90, 95% CI 0.86, 0.99, p < 0.001). Significant inverse association with 30 g of cheese per day (RR = 0.93, 95% CI 0.88, 0.99, p = 0.006)
Fats [27,28,33]		
	Zamora-Ros [27]	No significant association
	Shivappa [28]	40% increased CRC risk in high vs. low DII scores (RR = 1.40, 95% CI 1.26, 1.55, p < 0.001)
	Kim and Park [33]	No significant association with total fat (RR = 1.00, 95%CI 0.90, 1.12), saturated fat (RR = 0.97, 95%CI 0.86, 1.10), monounsaturated fat (RR = 1.08, 95%CI 0.92, 1.26), and polyunsaturated fats (RR = 0.99, 95%CI 0.93, 1.04)
Legumes [19,20]		
	Vieira [19]	No significant association
	Schwingshackl, et al. [20]	No significant association

cancer risk [22]. In this same study, beef increased CRC risk while pork had no association [22].

Another study recommended that intake of red meat should not exceed 500 grams per week as per guidelines from the National Food Agency in Sweden [23]. The study showed that pork incidence increased the incidence of colorectal cancer and beef increased the risk of rectal cancer in men [23]. An inverse CRC risk was noted in women in this Swedish prospective cohort study and high intake of beef was inversely associated with colon cancer [23].

Processed red meat consumption was positively associated with CRC risk, specifically with distal colon cancer at 30 and 50 g/day increase [21]. Unprocessed red meat was inversely associated with distal colon cancer at 1 serving per day of 100 and 120 gram increase [21].

Two studies did not show a significant association with red meats [17,18].

Poultry

Four studies were included that collectively showed no significant association between poultry consumption and colorectal cancer [18,19,22,23]. One study had no association at 100 grams per day [19]. Another study showed no significance at low, medium, or high intake [18].

One study showed no association with CRC but did show an inverse association with rectal cancer [22].

Seafood

Five studies were included and four show an inverse association and protective factor of fish [17,19,20,23,24]. Fish consumption had a reduced risk of CRC [24]. If one increases fresh fish by 20 g/d, there is a 2% reduction of developing a gastrointestinal cancer [24].

Fish decreased the colorectal cancer risk by 11% with 100 g/day [19]. There was a trend for an inverse association for 100 g/day of fish in another study [20]. A significant inverse association with rectal cancer was present with fish intake in one study [23].

Fruits

Six studies were included in this review. Some studies were specifically for fruit [19,20,25] while one only had results when fruits and vegetables were combined [26]. Two studies focused on flavonoids which are present in fruits such as apples, berries, and citrus [27,28].

In the studies focused solely on fruit, the results were mixed. One study showed an inverse association for fruit at 100 g/d [20]. The second study showed no association between fruit intake and colorectal cancer [19]. The third study focused on colorectal adenomas (CRA) which are precursors to CRC. This study showed a significant reduction in CRA risk with fruits at 100 g/day [25]. No statistical significance or association was found in the study combining fruit and vegetables at 100 g/day increase in intake [26].

In the flavonoid studies, one showed no statistical significance with CRC risk and in total flavonoid intake or flavonoid subclasses [27]. The other focused on dietary inflammatory index (DII) score, which is a low score in flavonoids. When comparing high vs. low DII, there was a 40% increase in CRC risk [28]. Higher scores in the (DII) were associated with colorectal cancer and each 1-point increase in the DII score led to an increased risk of CRC of 7% [28].

Vegetables

Five studies were included in this review. Two studies examined fruits and vegetables combined [25,26], two looked at vegetables [19,20], and one specifically looked at cruciferous vegetables, broccoli, and cabbage [29].

When examining the combination of fruits and vegetables at 100 g/day, there was no association with CRA [25]. At a 100 g/day increase in fruit and vegetable intake, there was no statistical significance [26].

There were mixed findings of vegetable intake of 100 g/day. There was no association between vegetables and CRA [25], but an inverse association with CRC risk was determined to exist [19,20].

When examining cruciferous vegetables (CV) and CRC risk, an inverse association occurred and was similar in cabbage and broccoli specifically [29]. When the studies were separated, this finding was seen better in the case-control studies, and only a borderline significance was observed in the prospective cohort studies.

Whole grains

Three studies comprised of systematic reviews and meta-analyses of prospective studies and randomized controlled trials evaluated whole grains in relation to CRC and all found an inverse association with CRC risk [19,20,30]. One study showed an association for every 15 g more per day [30]. The other two studies showed a decrease in CRC risk with 90 g and 30 grams of whole grains per day respectively [19,20].

Fiber

Four studies were analyzed that looked at prospective studies and meta-analyses of prospective cohort and case-control studies [26,28,30,31]. Three articles specifically examined fiber [26,30,31] while one examined DII scores [28], and all the studies showed protective factors against CRC.

One study showed significant inverse associations with total fiber intake and CRC risk and significance with cereal fiber, not fruit or vegetable fiber [26]. Total fiber intake showed an inverse association with CRC risk for every 8g more of fiber consumed per day with the greatest benefit at 25-29 g/day [30].

When looking at colon cancer location specifically, an inverse association for dietary fiber was demonstrated in high vs. low fiber intake in proximal colon cancers with a lower risk of 14% [31]. Distal colon cancer risk was 21% lower in the high vs. low fiber intake [31].

Fiber is one of the anti-inflammatory parameters, giving it a lower DII score. Higher scores in the DII were associated with colorectal cancer and each 1-point increase in the DII score led to an increased risk of CRC of 7% [28].

Dairy

Three studies consisting of reviews and meta-analyses with cohort and case-control studies evaluated dairy products and the correlation with CRC [19,20,32]. An inverse association was found for dairy at 200 g/d in two studies [20,32]. Another study found that higher dairy intake at 400 g/day decreased CRC risk [19].

Milk intake at 200 g/day had an inverse association with CRC as well [19,32].

One study found no association with cheese intake [19]. Another study found that 30 g of cheese per day had a significant inverse association with CRC [32].

Fats

One study directly evaluated dietary fat intake and CRC risk while two indirectly studied through DII score and flavonoids by analyzing systematic reviews and meta-analyses of prospective cohort and case-control studies. There was no significant association between CRC risk and total fat, saturated fat, monounsaturated fat, and polyunsaturated fats [33].

Monounsaturated and polyunsaturated fats have a low DII score, and one study showed that there was a 40% increased CRC risk in high vs. low DII scores [28]. Another study broke down flavonoid intake into subclasses and found no association in total flavonoid intake or the subclass of flavones, which contains two principal olive oil phenols [27].

Legumes

Two studies looked at legumes and CRC risk [19,20]. One found no association at 50 g/day [19], and the other had no association at 0-173 g/day [20].

Discussion

A Mediterranean diet focuses on fish, poultry, unsaturated fats, whole grains, fruits, vegetables, nuts, and legumes. A low-carbohydrate diet focuses on low-carbohydrate, high fat, and moderate protein with a variation in grams of carbohydrates consumed daily. Fish, red meats, poultry, eggs, oils, full-fat dairy, non-starchy vegetables, berries, nuts, and seeds are allowed while starchy vegetables and fruits, legumes, and whole grains are restricted.

The studies evaluating red meat consumption were fundamental in this review. Five of the seven studies showed an increased risk. The two that did not show an association were those focusing on the MedD as a whole and the relative risk for red meats was not provided in either [17,18]. The results of red meat intake in relation to CRC varied by location and in many of the cases was sometimes more significant in colon or rectal cancer than colorectal cancer [19,21,23].

Higher red meat consumption was associated with a higher BMI and a decrease in physical activity and fish consumption, calcium intake, and vitamin D intake [21]. While processed red meat consumption was positively associated with CRC risk, unprocessed red meat had a weak non-significant positive association [21]. This study also showed a protective factor between unprocessed red meat and distal colon cancer [21]. Similar findings occurred in women in a Swedish cohort study [23]. The study hypothesized that a more protective factor was seen in red meat in this study due to less antibiotics and growth factors in Swedish red meat.

There was a consensus that there was no association between poultry and CRC risk.

There was a consensus that fish had a protective factor against CRC. Fish decreased the risk of colorectal cancer by 11% [19]. Another study showed a 12% decrease in risk and that each 20 g/d increase in fish consumption would decrease the risk of gastrointestinal cancer by 2% [24]. This finding was not directly linked to CRC, however, as there are many different types of GI cancers. There was a 41% decreased risk in rectal cancer in a meta-analysis of cohort studies as well [23]. Like other food groups, significance was seen in rectal cancer but not necessarily for colorectal cancer.

Fruits had a lack of consensus and the studies that did show an inverse association were only borderline [20,25]. Each additional increase in fruits by 100 g/d was inversely associated with CRC with the most benefits being seem up to 200 g/d [20]. One of these studies did not evaluate CRC but CRA which are precursors [25]. Two of the articles used to evaluate fruit intake were focused on flavonoids which are present in apples, berries, and citrus fruits. There was no significance in the specific flavonoid subclasses in relation to CRC [27]. The highest flavonoid intake was associated with the lowest BMI, tobacco consumption, and processed meat intake, suggesting that higher flavonoid intake users may have healthier lifestyles [27]. Flavonoids have a low DII score because they have less inflammatory factors. In the study, there was a 40% CRC risk increase in the low vs. high DII score [28]. While the study showed the increased risk of CRC with a high vs. low DII score, there was no data specifically on relative risk and low DII score solely [28].

Vegetable intake in relation to CRC had mixed results. There was one study that showed an inverse association with cruciferous vegetables [29]. Of the five studies included, three solely focused on vegetable intake. One study which analyzed prospective cohort and case-control studies showed an inverse association with cruciferous vegetables [29]. When exclusively analyzing the cohort studies, only a borderline significance was established [29]. The other two studies also showed an inverse association with vegetable intake of 100 g/day [19,20]. After removing one study from the meta-analysis that had the most drive, no statistical association existed [19].

When examining the characteristics in the five vegetables studies, two did include vegetarians. Some of the participants in the EPIC study were recruited from Oxford in the United Kingdom where a large amount were health-conscious vegetarians. In the EPIC study, 31,546 participants were non-meat-eaters out of the approximate 470,000 participants [26]. The study on

cruciferous vegetables included 35 studies; twenty-five of these studies were on participants with no meat intake [29].

In many of these fruits and vegetable studies, the fruits and vegetables in the analyses were not specified [19,20,25,26]. When comparing a MedD and LCHF diet, the type of fruits and vegetables matter. LCHF diets only allow non-starchy fruits and vegetables.

There was a consensus that whole grains, fiber, and dairy products were protective factors against CRC. One study examining whole grains had a low sample size of 8,320 and only six studies, but all the studies showed an inverse association [19]. The risk of CRC was decreased by 20% when consuming 120 grams of whole grains per day [20]. These results were not statistically significant however. There was even borderline decreased risk at increasing whole grains by 15 grams per day which could indicate how protective it is since all other studies showed its protectiveness at 30 grams or higher [30].

Total fiber intake and cereal fiber intake, not vegetable or fruit fiber, showed a significant decrease in CRC risk [26]. Cereal fiber is what is present in whole grains. While comparing high vs. low fiber intake yielded a decreased colon cancer risk in both proximal and distal colon sites, these results were not significant [31]. Further studies on different types of fiber need to be evaluated, specifically more studies comparing cereal, vegetable, and fruit fiber.

Both high and low fat dairy intake of 200-400 g/d showed a decreased CRC risk [19,20,32]. The increase of dairy decreased the risk of CRC by 17% up to 400 g/day with additional benefits above this value [20]. Furthermore, 200 g/day of milk showed similar significant results [19,32]. The mechanism that dairy products work in reducing CRC may be the calcium intake as a prior study has shown that calcium through dairy products or supplementation both decreased CRC risk [20].

There was no consensus in the studies that evaluated fats. While only one of the three studies directly analyzed fats and their subtypes, it showed no significance. Prior studies have shown the benefits of monounsaturated and polyunsaturated fats in CRC. In this review, one study showed no association with CRC while the other had a negative association with monounsaturated and polyunsaturated fats which is similar to what other studies have shown [28,33]. Prior pooled analyses have showed that higher intake of fat is associated with CRC compared to lower intake [33]. When looking at different types of fat, another study showed that saturated fat and total fat can increase CRC risk [33].

Olive oil is categorized as a monounsaturated fat and is key in the Mediterranean diet. It contains many compounds, including flavonoids, that are individually shown to have favorable effects on inflammation, gut microbial, and carcinogenesis [34]. There are, however, no human studies or clinical trials supporting this; it is based on animal studies and *in vitro* models only.

DII score was only explored in one study included in this review in relation to CRC risk. While there was a 40% increased CRC risk with a higher DII score, these significant findings were not for a specific food [28]. Higher DII scores occur in pro-inflammatory foods such as carbohydrates, protein, total fat, iron, cholesterol, and saturated fat. Lower DII scores are seen in anti-inflammatory foods such as flavonoids (apples, berries, citrus fruits, legumes), monounsaturated and polyunsaturated fats, vitamins, and fiber. These significant findings may show the importance of incorporating DII scores into diets more, which the Mediterranean diet is essentially already doing.

A limitation of this literature review was looking at only colorectal cancer cases. Some studies did not differentiate between CRC, colon, and rectal cancers while others looked at CRC as a whole and then evaluated individual sites and genders as well. Moreover, many studies did not define the specific foods in their studies; fruits and vegetables were rarely broken down and if they were, it was said that no significance existed and we were never given the individual statistics.

Furthermore, there were multiple studies that published results of a food group with a positive or inverse association and CRC, but there was no statistical significance present or the p-value was not included [17,19,20,22,23,25,30,31].

Based on these studies under review, the main differences in the two diets are red meat, whole grains, starchy versus non-starchy fruits and vegetables, and legumes. The two with a consensus are red meat, which increases CRC risk and whole grains which decreases CRC risk. Whole grains are in the Mediterranean diet but restricted in LCHF diets. Red meats are in the LCHF diets but allowed in moderation in the Mediterranean diet. Based on this analysis, it would be assumed that the Mediterranean diet is better for you than LCHF diet in regards to CRC. Neither diet can prove superior in reducing CRC risk in this review since no data on LCHF diets could specifically be found.

The consensus is that the Mediterranean diet decreases colorectal cancer risk when high adherence is obtained [17]. When adjusting for age, body mass index, physical activity, smoking status, socioeconomic status, and family history of colorectal cancer, high adherence reduced the risk of CRC by 12% [18]. Low-carbohydrate diets in relation to CRC risk and incidence are unknown. Studies in this review evaluated specific food groups in both diets. Based on the findings, it is recommended that those who use a LCHF diet modify to decrease the amount of red meat consumption to less than 50

grams per day and increase chicken and fish for protein. Neither diet can be shown to be superior in reducing CRC risk in this review.

Further studies need to focus specifically on a LCHF diet with CRC. Fruits and vegetables need to explicitly be looked at, especially starchy versus non-starchy. Furthermore, studies on unprocessed red meat should be performed in more detail, specifically grass-fed, organic beef since there are antibiotics and growth factors in the standard American meat. Moreover, human studies on olive oil and more studies on dietary fiber should be explored. Future studies should better evaluate a LCHF diet in comparison with Mediterranean diet in relation to colorectal cancer risk.

Conclusion

Colorectal cancer risk is decreased with fish, whole grains, dietary fiber, and dairy products. Increased consumption of red meats increases the risk of colorectal cancer as is supported in prior research studies; however, in this review, studies were mixed. There are mixed studies on fruit and vegetable intake in relation to CRC risk. It appears that cruciferous vegetables could decrease colorectal cancer risk. There is no association in our studies with poultry, legumes, or fats; however, previous studies have shown the benefit of legumes and fats, specifically polyunsaturated fats and monounsaturated fats, which are in olive oil and important in the Mediterranean diet. A high dietary inflammatory index score appears to be associated with increased CRC risk, but more research on this needs to occur.

While the literature indicates a benefit from the Mediterranean diet in reducing the risk of colon cancer, studies on a low-carbohydrate diet, such as the Atkins or ketogenic diets, show the incidence of colorectal cancer are less common. The low-carbohydrate diet should limit the amount of red meat allowed. If a person is participating in a reduced-carbohydrate diet, they should be aware of which foods can increase risk of colon cancer and modify the diet to avoid these.

There is research on certain foods that increase the risk of colon cancer or have a protective factor against it, but there is limited research comparing diets. Further studies need to better evaluate a LCHF diet in comparison with Mediterranean diet in relation to colorectal cancer risk. There needs to be studies directly evaluating LCHF diets to cancer risk as the current research are limited.

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Conflicts of Interest

The author declares no conflicts of interest.

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