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Colon Cancer: What We Eat

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Synopsis

A higher incidence of colorectal cancer (CRC) is observed in Oceania and Europe, whereas Africa and Asia have a lower incidence. CRC is largely preventable by adapting a healthy lifestyle, such as healthy diet, adequate physical activity, and avoiding obesity. This review summarizes the latest work available, mainly epidemiologic studies, to examine the relationship between diet and CRC. Higher intake of red/processed meat could increase the CRC risk, while fibers, especially from whole-grains and cereals, as well as fruit and vegetables may decrease the CRC risk. However, heterogeneity and inconsistency among studies or individuals need to be taken into consideration.

Keywords

Colorectal cancer; diet; red/processed meat; fish; fiber; fruit and vegetables; vitamins and minerals; coffee and tea

Introduction

Cancer is the second leading cause of death worldwide, having caused 8.8 million deaths in 2015[1]. Among all cancers, colorectal cancer (CRC) is the third-most common cancer in men (accounting for 10% of all male cancers) and the second in women (accounting for 9.2% of all female cancers)[2]. The estimated age-standardized incidence rate of CRC is 20.6 per 100,000 for men and 14.3 per 100,000 for women, and the mortality rate is 10.0 for men and 6.9 for women[2]. A higher incidence of CRC is observed in Oceania and Europe, ranging from 30 or more per 100,000, whereas Africa and Asia have a lower incidence, at less than 5

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per 100,000[3,4]. Countries with the highest economic development are likely to have higher incidences and mortality rates, and these are rising in countries becoming more developed[2].

CRC is largely preventable. The higher incidence in more developed countries can be attributed, at least partially, to the Western lifestyle, with its high intake of red and processed meat, which has been reported to associate positively with higher risk of CRC[5,6]. The global cancer reports published by the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) in 2007 and updated in 2011 listed red and processed meat as "convincing" factors that increase the risk of CRC[4,7]. Many other dietary factors, such as fiber, fruit, and vegetables, may associate inversely with CRC risk[4,7].

This review aims to summarize the latest work available, mainly epidemiologic studies, to examine the relationship between diet and CRC. The largest studies of dietary consumption and CRC risk conducted worldwide include the National Institutes of Health-American Association for Retired Persons Diet and Health Study (NIH-AARP DHS), the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO), the Nurses' Health Study (NHS), the Health Professionals Follow-up Study (HPFS), and the Physicians' Health Study (PHS) from the United States. From Europe, we included the European Prospective Investigation into Cancer and Nutrition (EPIC), and from Asia we selected the Japan Public Health Center-based Prospective Study (JPHC Study) and the Shanghai Women's Health Study (SWHS). Many other regional studies have also added to our understanding of the diet–CRC interaction.

Materials and Methods

We conducted a PubMed search for human studies published up to 2017, using the key words: colorectal cancer, diet, nutrition, and epidemiology. We gave preference to studies that reported risk estimates (hazards ratio (HR), odds ratio (OR), relative risk (RR), or incidence rate ratio (IRR)) of CRC as well as measures of variability (95% confidence interval (CI)). Articles and clinical trials that described and compared the impact of diets on CRC were first screened according to abstracts and titles; then the full-text articles were assessed for eligibility. Reference lists from the studies selected by the electronic search were manually searched to identify further relevant reports. Reference lists from all available review articles and primary studies were also considered. Our analysis included only the most common foods across different cultures, including meat, fish, dietary fiber, fruit and vegetables, vitamins and minerals, and coffee and tea.

Content

Red meat and processed meat—During the past three decades, many large epidemiologic studies have investigated the association of red/processed meat with the risk of CRC. Although these studies varied in terms of analytic model, gender, sub-location of the tumor, and meat subtype, the majority observed a positive association of high intake of red/processed meat with the risk of developing CRC[8–17]. Therefore, the WCRF/AICR listed red/processed meat as "convincing" factors for increasing CRC risk[4,7].

The NIH-AARP DHS analyzed about 500,000 participants aged 50–71 years at baseline (1995–1996), and followed them until the end of 2003, using a 124-item food frequency questionnaire (FFQ). Individuals in the highest quintile, compared with those in the lowest quintile, of red meat (HR: 1.24, 95% CI: 1.12–1.36, *p*-trend <0.001) and processed meat (HR: 1.20, 95% CI: 1.09–1.32, *p*-trend <0.001) intake had an increased risk of CRC. The positive association for both types of meat was more robust for rectal cancer than for colon cancer[18,19].

The PLCO study was a large population-based randomized trial of 154,952 participants aged 55–74 years in 1993. The subjects were randomly assigned to an intervention arm with trial screening or a control arm with standard care, and they were followed for 6 years, using a 137-item FFQ. Some suggestive positive associations of red meat (OR: 1.22, 95% CI: 0.98–1.52, *p*-trend =0.12) and processed meat (OR: 1.23, 95% CI: 0.99–1.54, *p*-trend =0.12) were observed when the highest quartiles were compared to the lowest quartiles[20].

The NHS included 121,700 U.S. female registered nurses aged 30–55 years in 1976, and the HFPS included 51,529 U.S. male healthcare professionals (dentists, pharmacists, optometrists, osteopaths, podiatrists, and veterinarians) aged 40–75 years in 1986. These two large studies used a 131-item FFQ every 4 years until they ended in 2010. Only higher intake of processed red meat associated significantly with a higher risk of distal colon cancer in both age-adjusted and multivariable-adjusted models (HR: 1.36, 95% CI: 1.09–1.69, *p*-trend =0.006). Interestingly, unprocessed red meat intake associated inversely with the risk of distal colon cancer (HR: 0.75, 95% CI: 0.68–0.82, *p*-trend <0.001), but only after adjustments for calcium, folate, and fiber intake. No significant gender difference was observed[21].

The EPIC study was one of the largest cohort studies worldwide: 366,521 women and 153,457 men aged 35–70 years at baseline (1992–1998) from 10 European countries were followed for almost 15 years. Red and processed meat associated significantly with increased CRC risk (HR: 1.35, 95% CI: 0.96–1.88, *p*-trend =0.03), but the associations were not significant in specific sub-locations of tumors[22]. After correction for measurement errors, red and processed meat intake significantly associated with higher CRC risk (HR: 1.55, 95% CI: 1.19–2.02, *p*-trend =0.001)[22].

The JPHC Study involved two cohorts with a total of 46,026 men and 52,485 women aged 45–74 years in 1995–1998. The participants were surveyed with a 138-item FFQ until 2006. The analysis found statistically significant positive associations between higher intake of red meat (HR: 1.48, 95% CI: 1.01–2.17, *p*-trend =0.03) and beef (HR: 1.62, 95% CI: 1.12–2.34, *p*-trend =0.04) with colon cancer risk in women. In particular, higher intake of beef associated positively with risk of proximal colon cancer in women (HR: 2.52, 95% CI: 1.53–4.14, *p*-trend =0.01) and with distal colon cancer in men (HR: 1.36, 95% CI: 0.90–2.06, *p*-trend =0.04). No significant association was observed between processed meat and risk of CRC[23].

In the SWHS, about 75,000 women aged 40–70 years in 1997–2000 were surveyed by an FFQ every 2 years until the end of 2005. Neither total meat intake nor red meat intake

associated with the risk of CRC cancer. This study also compared the various popular cooking methods in China, such as deep frying, stir frying, roasting, smoking, and salting. Only smoking associated positively with risk of CRC (RR: 1.4, 95% CI: 1.1– 1.9, *p*-trend =0.01)[24].

Some regional studies produced inconsistent results, however. For example, the Danish Diet, Cancer and Health cohort study (DCH), which was part of the overall EPIC study (though EPIC included only 18% of this Danish cohort), found no overall significant association between red/processed meats with risk of CRC. The only positive associations were between lamb and colon cancer (IRR: 1.35, 95% CI: 1.07–1.71, *p*-trend =0.01) and pork and rectal cancer (IRR: 1.63, 95% CI: 1.11–2.39, *p*-trend =0.03). Interestingly, there was a significant negative association between beef and rectal cancer (IRR: 0.75, 95% CI: 0.52–1.09, *p*-trend =0.03)[25].

The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study in Finland found no significant associations between meat, different types of meat, or fried meat and risk of CRC[26]. The Melbourne Collaborative Cohort Study (MCC) in Australia observed no significant associations between red/processed meat and the risk of CRC[27]. On the other hand, the Swedish Mammography Cohort (SMC) observed a significant positive association between red meat intake and risk of distal colon cancer (RR: 2.22, 95% CI: 1.34–3.68, *p*-trend =0.001)[28]. A Canadian case-control study reported increased risk of both colon cancer (OR: 1.5, 95% CI: 1.2–1.8, *p*-trend <0.0001) and rectal cancer (OR: 1.5, 95% CI: 1.2–2.0, *p*-trend =0.001) with higher intake of processed meat[29,30].

In summary, currently available epidemiologic evidence indicates positive associations between red/processed meat and CRC risk, though it does not rule out contributions from other confounding factors, such as higher fat intake and lack of physical activity. The associations tend to be stronger for rectal cancer than colon cancer and for processed meat than red meat, as well as for men than women. Potential underlying mechanisms of the elevated CRC risk by red/processed meat include carcinogenic chemical by-products made during cooking and processing, such as heterocyclic amines, polycyclic aromatic hydrocarbons, and N-nitroso compounds. However, controlled studies need to delineate the mechanisms of action of these carcinogenic chemicals. Characteristics of studies of red/processed meat intake and CRC risk are shown in Table 1.

Fish

Fish consumption may decrease the risk of CRC development, partially because fish contains high levels of polyunsaturated fatty acids (PUFAs). Although many epidemiologic studies have examined the possible association between fish consumption and risk of CRC, highly inconsistent results among studies were reported 31,32. Therefore in 2011, the WCRF/AICR changed fish consumption from “suggestive” to “no conclusion”[4,7].

The EPIC study observed significantly inverse associations between fish consumption and the risk of CRC (HR: 0.69, 95% CI: 0.54–0.88, *p*-trend <0.001). The trend for this inverse association was due mainly to the decreased risk for the left side of the colon (*p*-trend =0.02) and for the rectum (*p*-trend <0.001)[22].

The PHS also revealed significantly inverse associations between fish intake and the risk of CRC (RR: 0.63, 95% CI: 0.42–0.95, *p*-trend =0.02). More importantly, this inverse association was not due solely to the substitution of fish for red meat[33], suggesting that fish has a potentially protective effect.

However, three large U.S. prospective studies found no significant overall associations. The NHS and HPFS found no overall association between fish, ω-3, or ω-6 PUFA intake and CRC. Surprisingly, ω-3 PUFA, such as a-linolenic acid (ALA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and docosapentaenoic acid (DPA), which are generally considered to protect against cancer, associated positively with risk of CRC in the NHS (HR: 1.36, 95% CI: 1.03–1.80, *p*-trend =0.04)[34]. The NIH-AARP DHS reported no significant association between fish intake and risk of CRC[35].

Similarly, many regional studies showed mixed results. For example, no associations were observed in the ATBC study[26] in Finland, the Japan Collaborative Cohort (JACC) Study[36] and the Ohsaki Cohort study[37] in Japan, the SMC study[28] in Sweden, the Oxford Vegetarian Study[38] in the United Kingdom, the Norwegian Women and Cancer (NOWAC) study[39] in Norway, or a Canadian population-based case-control study[30]. A significant lower risk of CRC was observed in Finnish professional fishermen and their wives, who consume large amounts of fish, but that might have been due to their high physical activity during fishing[40]. While no association was observed between total fish intake and the risk of CRC in the SWHS in China, higher consumption of eel (*p*-trend = 0.01) and shellfish (*p*-trend = 0.04) were found to increase the risk of CRC[24]. High levels of arachidonic acid (AA), a ω-6 PUFA, also associated with a higher risk of CRC (RR: 1.39, 95% Cl: 0.97–1.99, *p*-trend =0.03)[41].

Encouragingly, one meta-analysis that pooled 27 prospective cohort studies observed a moderate but significant reduction in the risk of CRC (RR: 0.93, 95% Cl: 0.87–0.99, *p*-trend <0.01)[31], and the association was stronger for rectal cancer (RR: 0.85, 95% Cl: 0.75–0.95) than for colon cancer (RR: 0.95, 95% Cl: 0.91–0.98). Another meta-analysis that pooled 22 prospective cohorts and 19 case-control studies observed a 12% decrease in the risk of CRC with the highest fish intake (OR: 0.88, 95% Cl: 0.80–0.95)[32]. However, both analyses found significant (*p* <0.001) heterogeneity among the included studies, suggesting the contribution of other confounding factors and possible non-responsiveness to fish consumption. Collectively, understanding the mechanisms of how PUFAs might benefit human health could explain the non-responsiveness in some studies. Fish oil, which is rich in EPA and DHA, was reported to improve cancer patients' quality of life[42], suggesting that it might be a useful dietary supplement for CRC patients on standard therapies. Characteristics of studies of fish intake and CRC risk are shown in Table 2.

Fibers from all sources

In 1969, Burkitt proposed that high fiber consumption might reduce the risk of CRC after observing that African blacks who consumed a high-fiber/low-fat diet had a lower incidence of colon cancer and mortality than their white counterparts who ate a low-fiber/high-fat diet[43]. Fiber includes heterogeneous plant material composed of cellulose, hemicellulose, and pectin[10]. Its potential protective effects include reducing fecal transit time, diluting fecal

carcinogens, affecting bile acid metabolism, maintaining colonic epithelial cell integrity, absorbing heterocyclic amines, and stimulating bacterial anaerobic fermentation to promote the production of short-chain fatty acids (SCFAs)[10,16]. SCFAs, such as acetate, propionate, and butyrate, have been shown to decrease colonic pH[44,45] and inhibit colon carcinogenesis[46–50].

Pooling multiple studies (one meta-analysis of 13 case-control studies[51], one analysis of 25 prospective studies[52], and one analysis of 16 case-control and 4 cohort studies[53]) uncovered significant inverse associations between dietary fiber intake and risk of CRC, but this association was not seen in the Pooling Project of Prospective Studies of Diet and Cancer[54]. In addition, some individual large prospective studies, including the EPIC study (RR: 0.83, 95% CI: 0.72–0.96, *p*-trend =0.013)[55,56] and the PLCO study (for distal colon cancer: HR: 0.62, 95% CI: 0.41–0.94, *p*-trend =0.03)[57], observed significant inverse associations, which were not seen in others, such as the NHS, the HPFS[58], and the Women's Health Study (WHS)[59]. Interestingly, even in the same populations, different studies showed discrepant results. For example, a case-control study in China[60] observed a significant inverse association between total dietary fiber and the risk of CRC (OR: 0.38, 95% CI: 0.27–0.55, *p*-trend <0.01), while the prospective SWHS in China[61] showed no significant results. Similarly, the JACC Study in Japan[62] reported a significant decreasing trend of dietary fiber intake with the risk of colon cancer (RR: 0.73, 95% CI: 0.51–1.03, *p*-trend =0.028), while the JPHC study in Japan[63] showed no association. Methodological differences might be one reason. For example, one case-control study within seven UK cohort studies reported a significant inverse association when food diaries, but not FFQs[64], were used. Food diaries may provide more details of dietary intake, while FFQs provide only a short list (100–200 items) that combines several sources into one category. However, food diaries may introduce greater bias and measurement error into a study. Therefore, confounding factors and limitations in study design need to be considered when interpreting results from either individual studies or pooled meta-analyses.

Fiber from whole grains and cereals

Whole-grains and cereals are major sources of dietary fiber, and accumulating evidence suggests that high fiber intake from whole grains and cereals associates with a lower risk of CRC. This association was seen in the EPIC study (cereals: RR: 0.87, 95% CI: 0.77–0.99, *p*-trend =0.003)[55], the NIH-AARP DHS (grain: RR: 0.51, 95% CI: 0.29–0.89, *p*-trend =0.01)[65], and the Scandinavian HELGA study (whole-grain wheat: IRR: 0.65, 95% CI: 0.50–0.84)[66,67]. The HELGA study included three prospective cohorts: the NOWAC study, the Northern Sweden Health and Disease Study (NSHDS), and the DCH study. In Scandinavia, whole-grain food consumption is relatively high. However, no consistent associations were observed within individual studies[68,69]. One analysis that used plasma alkylresorcinol concentration (a biomarker of whole-grain wheat and rye intake) alone or combined with FFQ showed inverse associations with distal colon cancer, but using only an FFQ was not powerful enough[70]. Accordingly, these studies suggest a decreasing trend between high intake of fiber from whole-grains and cereals with the risk of CRC. Characteristics of studies of fiber intake and CRC risk are shown in Table 3.

Fruit and vegetables

Fruit and vegetables, which are rich in polyphenol compounds, flavonoids, soluble fiber, vitamins, and minerals, have been highly recommended for CRC prevention, though the results of epidemiologic studies are weak, possibly because of the variability within the category "fruit and vegetables."[10,11,15,16,36] The WCRF/AICR listed fruit and vegetables as "suggestive" factors for decreasing CRC risk[4].

The EPIC study observed a lower risk of CRC with higher consumption of fruit and vegetables combined (HR: 0.86, 95% CI: 0.75–1.00, *p*-trend =0.04)[55,71]. Further analysis found that this association was dependent on smoking status: the association was inverse in never and former smokers, while it became positive in current smokers[71]. However, when dietary consumption was converted into flavonoid intake, no association was observed[72].

The NHS and HPFS also examined flavonoid intake, and found no significant association with CRC[73]. In another US study, the NIH-AARP DHS, which used servings/1,000 kcal per day for analysis, observed a significantly reduced risk of CRC for the highest intake of vegetables among men (RR: 0.82, 95% Cl: 0.71–0.94, *p*-trend =0.03), mainly from distal colon cancer (RR: 0.76, 95% Cl: 0.59–0.98, *p*-trend =0.04). Interestingly, a significantly increased risk of rectal cancer for the highest intake of fruit among women was also observed (RR: 1.59, 95% Cl: 1.04–2.44, *p*-trend =0.01). When subtypes of vegetables were considered, green leafy vegetables associated with a lower risk of CRC among men (RR: 0.86, 95% Cl: 0.74–0.99, *p*-trend =0.04)[74].

Although some regional studies have reported non-significant results, including the Netherlands Cohort Study–Meat Investigation Cohort (NLCS–MIC)[75,76], the Western Australian Bowel Health Study[77], and a meta-analysis in a Japanese population[78], pooled studies resulted in a week decreasing trend between higher consumption of fruit and vegetables and the risk of CRC[79,80]. Promisingly, a meta-analysis that focused only on cruciferous vegetables and included 24 case–control and 11 prospective studies found a significantly inverse association (RR: 0.82, 95% Cl: 0.75–0.90) between cruciferous vegetables intake and the risk of CRC[81].

Some studies have classified subjects as vegetarians (including vegan lacto-ovo vegetarian, pesco-vegetarian, and semi-vegetarian) and non-vegetarians. The Adventist Health Study (AHS) II observed an overall lower risk of CRC among vegetarians than in non-vegetarians (HR: 0.78, 95% Cl: 0.64–0.95, *p*-trend =0.01), particularly pesco-vegetarians (HR: 0.57, 95% Cl: 0.40–0.82, *p*-trend =0.002)[82]. After combining 6 cohort studies, a meta-analysis found that the association between a vegetarian diet and the risk of CRC was not significant[83]. However, semi-vegetarians and pesco-vegetarians showed a lower risk of CRC[83]. This potential protection observed in pesco-vegetarians might be due to the beneficial effects of fish consumption. Interestingly, the EPIC-Oxford study reported an opposite trend: a higher incidence in vegetarians than in non-vegetarians (IR: 1.49, 95% Cl: 1.09–2.03) or meat eaters (IR: 1.39, 95% Cl: 1.01–1.91)[84].

Accordingly, higher consumption of fruit and vegetables might have the potential to decrease the risk of CRC. However, more research is needed to explain the heterogeneity

among studies. Many factors easily influence the outcomes of analyses, such as the way food intake is measured, analytic method, and other confounding factors. It is also highly debatable whether an analysis should accept “fruit and vegetables” as a category or delineate it into subtypes. Characteristics of studies of intake of fruit and vegetables and CRC risk are shown in Table 4.

Vitamins and minerals

Vitamins and minerals are important micronutrients that support our bodies and benefit our health. However, the relationship between their intake and disease is far from clear. A Canadian study observed overall beneficial effects of multiple vitamins (OR: 0.7, 95% CI: 0.4–1.3, *p*-trend =0.03), B-complex vitamins (OR: 0.4, 95% CI: 0.2–0.7, *p*-trend =0.0005), vitamin E (OR: 0.6, 95% CI: 0.4–0.9, *p*-trend =0.002), calcium (OR: 0.4, 95% CI: 0.3–0.6, *p*-trend <0.0001), iron (OR: 0.6, 95% CI: 0.4–1.0, *p*-trend =0.03), and zinc (OR: 0.4, 95% CI: 0.2–0.9, *p*-trend =0.03) against distal colon cancer among women taking these nutrients as supplements[85].

However, one could argue that more is not always better[86] and that a balanced combination with the right doses would maximize the beneficial effects. For example, the MCC study obtained very interesting results after analyzing the risk of CRC with dietary intake of B vitamins, finding a U-shaped association between vitamin B_6 and colon cancer and an inverse U-shaped association between vitamin B_{12} and rectal cancer[87]. Vitamin B_6 was also found to significantly increase the risk of rectal cancer among Dutch women (RR: 3.57, 95% CI: 1.56–8.17, *p*-trend =0.01)[88]. However, folate, a form of vitamin B, was shown to associate with a lower risk of CRC in the DCH study (IRR: 0.83, 95% CI: 0.57–1.21, *p*-trend =0.04)[89]. This association was significant only when the vitamin was obtained from the diet but not from supplements[89].

Several studies have suggested that magnesium seems to associate with a lower risk of CRC[90–93]. Calcium was shown to reduce the risk of CRC in some studies[94,95], but it did not correlate with vitamin D[94,96]. Characteristics of studies of intake of vitamins and minerals and CRC risk are shown in Table 5.

Coffee and tea

Although coffee and tea are popular worldwide, only a few studies have investigated their effects on the risk of CRC. One meta-analysis of 41 prospective studies[97] and another of 87 databases[98] found no significant associations between tea consumption and the risk of CRC. Several other regional studies also reported non-significant results 99–102. The SWHS showed a dose-response relationship between green tea consumption and a lower risk of CRC[103], while the Singapore Chinese Health Study observed an increased risk of CRC among male green tea drinkers[104]. The subjects in these two studies are generally considered the same (Chinese), which may suggest a gender difference in response to green tea. In addition, other confounding factors also affect the results. For example, the NIH-AARP DHS found an inverse association between the risk of proximal colon cancer with both caffeinated coffee and decaffeinated coffee, but the subjects who drank decaffeinated coffee

happened to consume less alcohol, fewer calories, less red meat, and more fruit and vegetables. However, they also exercised less and smoked more[102].

Summary/Discussion

Does cancer occur because of genes, environmental factors, or merely bad luck[105]? A surprisingly high correlation (r =0.80) was observed between normal stem cell divisions and cancer incidence in an analysis of 17 different cancer types in 69 countries, representing 4.8 billion people[106]. For colon cancer, 26.1% of the driver gene mutations were induced by the environment (E), only 2.5% were heredity (H), and the remaining 71.4% were attributable to random mistakes during normal DNA replication (R)[106]. Although one could argue that this was only a statistical analysis and that the model might be too ideal, this randomness might explain the heterogeneity and inconsistency among studies or even individuals.

In the current review, we focused mainly on large prospective studies and meta-analyses. Our literature research basically supports the WCRF/AICR's recommendations[4,7], while some variants exit, especially to dietary fiber, a complex substance that is difficult to define. Our review is also limited, as the WCRF/AICR's cancer reports include many more studies. In addition, all studies are subject to design bias and measurement errors to a certain degree. Therefore, results from different studies should be carefully interpreted and compared.

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Abbreviations

AHS	Adventist Health Study
AICR	American Institute for Cancer Research
ATBC	Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study
CI	confidence interval
CRC	colorectal cancer
DCH	Danish Diet, Cancer and Health cohort study
EPIC	European Prospective Investigation into Cancer and Nutrition
FFQ	food frequency questionnaire
HPFS	Health Professionals Follow-up Study
HR	hazard ratios
IRR	incidence rate ratios
JACC	Japan Collaborative Cohort

JPHC	Japan Public Health Center-based Prospective Study
MCC	Melbourne Collaborative Cohort
NHS	Nurses' Health Study
NIH-AARP DHS	National Institutes of Health-American Association for Retired Persons Diet and Health Study
NLCS	Netherlands Cohort Study
NOVAC	Norwegian Women and Cancer
NSHDS	Northern Sweden Health and Disease Study
OR	odds ratios
PHS	Physicians' Health Study
PLCO	Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial
RR	relative risk
SMC	Swedish Mammography Cohort
SWHS	Shanghai Women's Health Study
WCRF	World Cancer Research Fund
WHS	Women's Health Study

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Key Points

- Colorectal cancer has a higher incidence in Oceania and Europe, and a lower incidence in Africa and Asia.
- Colorectal cancer is largely preventable by adapting a healthy lifestyle including healthy diet, adequate physical activity, and avoiding obesity.
- What we eat affects our risk of developing colorectal cancer: red/processed meat could increase the risk while fibers, fruit and vegetables may decrease the risk.
- Other foods, such as fish, vitamins and minerals, and coffee, might have potential effects on our risk of developing colorectal cancer.

Table 1

Characteristics of studies of red/processed meat and CRC

Study	Number of study participants	Age of participants	Follow-up years	CRC incidence	Analytic category	Analytical comparison, high versus low intake	Relative risk (95% CI)	Ref
NIH-AARP DHS	294,724 men and 199,312 women	50–71	1995–2003	5,107 (CRC)	Red meat	62.7 g/1000 kcal versus 9.8 g/1000 kcal	CRC: 1.24 (1.12–1.36), p<0.001	Ref ([18])
					Processed meat	22.6 g/1000 kcal versus 1.6 g/1000 kcal	CRC: 1.20 (1.09–1.32), p<0.001	
HPFS and NHS	47,389 men and 87,108 women	40–75/30–55	1986–2010/1980–2010	1,968 (Colon), 589 (Rectum)	Processed red meat	>5 servings/week verse 0	Distal colon cancer: 1.36 (1.09–1.69), p=0.006	Ref ([21])
					Unprocessed red meat	>5 servings/week verse 0	Distal colon cancer: 0.75 (0.68–0.82), p<0.001	
EPIC	47,8040 men and women	35–70	1992–2002	855 (Colon), 474 (Rectum)	Red and processed meat	≥160 g/day versus <10 g/day	CRC: 1.35 (0.96–1.88), p=0.03	Ref)[22])
						per 100 g increase	CRC: 1.55 (1.19–2.02), p=0.001	
JPHC	80,658 men and women	45–74	1995–2006	788 (Colon), 357 (Rectum)	Red meat	≥93 g/day versus <14 g/day	Women-Colon cancer: 1.48 (1.01–2.17), p=0.03	Ref ([23])
					Beef	≥28 g/day versus <0.1 g/day	Women-Colon cancer: 1.62 (1.12–2.34), p=0.04	
							Women-Proxima colon cancer: 2.52 (1.53–4.14), p=0.01	
						≥34 g/day versus <0.2 g/day	Men-Distal colon cancer: 1.36 (0.90–2.06), p=0.04	
SWHS	73,224 women	40–70	1997–2005	236 (Colon), 158 (Rectum)	smoking method of cooking	ever versus never	Colon cancer: 1.4 (1.1–1.9), p=0.01	Ref ([24])
DCH	25,832 men and 28,156 women	50–64	1993–2009	644 (Colon), 345 (Rectum)	Lamb	>8 g/day versus ≤5 g/day	Colon cancer: 1.35 (1.07–1.71), p=0.01	Ref (25)
					Pork	>54 g/day versus ≤27 g/day	Rectal cancer: 1.63 (1.11–2.39), p=0.03	
					Beef	>45 g/day versus ≤22 g/day	Rectal cancer: 0.75 (0.52–1.09), p=0.03	
SMC	61,433 women	40–75	1987–2003	389 (Colon), 230 (Rectum)	Red meat	≥94 g/day versus <50 g/day	Distal colon cancer: 2.22 (1.34–3.68), p=0.001	Ref ([28])

Study	Number of study participants	Age of participants	Follow-up years	CRC incidence	Analytic category	Analytical comparison, high versus low intake	Relative risk (95% CI)	Ref
Case-control	–	20–76	–	1,727 (Colon), 1,447 (Rectum), 5,039 (Control)	Processed red meat	≥5.42 servings/ week verse ≤0.94 servings/week	Colon cancer: 1.5 (1.2–1.8), p<0.0001	Ref ([29])
							Rectual cancer: 1.5 (1.2–2.0), p=0.01	
ATBC	27,111 men (all smokers)	50–69	1985–1993	185 (CRC)	Total red meat	≥203 g/day versus <79 g/day	non-significant associations	Ref ([26])
					Processed meat	≥122 g/day versus <26 g/day	non-significant associations	
PLCO	17,072 men and women	55–74	1993–2001	1,008 (Distal colorectal adenoma)	Red meat	60.1 g/1000 kcal versus 13.5 g/1000 kcal	non-significant associations	Ref ([20])
					Processed meat	15.5 g/1000 kcal versus 1.5 g/1000 kcal	non-significant associations	
MCC	37,112 men and women	40–69	1990–1994	283 (Colon), 169 (Rectum)	Fresh red meat	>6.5 times/week verse <3 times/ week	non-significant associations	Ref ([27])
					Processed meat	>4 times/week verse <1.5 times/ week	non-significant associations	

Table 2

Characteristics of studies of fish and CRC

Study	Number of study participants	Age of participants	Follow-up years	CRC incidence	Analytic category	Analytical comparison, high versus low intake	Relative risk (95% CI)	Ref
EPIC	47,8040 men and women	35–70	1992–2002	855 (Colon), 474 (Rectum)	Fish	≥80 g/day versus <10 g/day	CRC: 0.69 (0.54–0.88), p<0.001	Ref ([22])
PHS	21,406 men and women	40–84	1982–1995	500 (CRC)	Fish	≥5 times/ week verse <1 time/ week	CRC: 0.63 (0.42–0.95), p=0.02	Ref ([33])
Finnish fishermen cohort	6410 men and 4,260 women	–	1980–2011	79 (Colon), 68 (Rectum)	Fish	–	Men-Colon cancer: 0.72 (0.52–0.98)	Ref ([40])
SWHS	73,242 women	40–70	1997–2005	396 (CRC)	Arachidonic acid	≥0.09 g/day verse <0.02 g/day	CRC: 1.39 (0.97–1.99), p=0.03	Ref ([41])
SWHS	73,224 women	40–70	1997–2005	236 (Colon), 158 (Rectum)	Eel	≥0.35 g/day verse 0	CRC: 1.3 (0.9–1.7), p=0.01	Ref ([24])
					Shellfish	≥0.6 g/day verse 0	CRC: 1.3 (1.0–1.6), p=0.04	
22 prospective cohort and 19 case-control studies	–	–	–	–	Fish	–	CRC: 0.88 (0.80–0.95)	Ref ([32])
27 prospective cohort studies	2,325,040 men and women	–	–	–	Fish	–	CRC: 0.93 (0.87–0.99)	Ref ([31])
							Colon cancer: 0.95 (0.91–0.98)	
							Rectal cancer: 0.85 (0.75–0.95)	
HPFS and NHS	47,143 men and 76,386 women	40–75/30–55	1986–2010/1980–2010	1,773B (Colon), 525 (Rectum), 158 (Unspecific)	Fish	Men: ≥46 g/day verse <16 g/day	non-significant associations	Ref ([34])
						Women: ≥40 g/day verse <15 g/day		
					Marine ω-3	≥0.3 g/day verse <0.15 g/day	Women-Distal colon cancer: 1.36 (1.03–1.80), p=0.04	

Study	Number of study participants	Age of participants	Follow-up years	CRC incidence	Analytic category	Analytical comparison, high versus low intake	Relative risk (95% CI)	Ref
NIH-AARP DHS	293,466 men and 198,720 women	50–71	1995–2003	5,095 (Colon), 1,884(Rectum)	Fish	≥21.4 g/100 kcal verse <3.6 g/1000 kcal	non-significant associations	Ref ([35])
ATBC	27,111 men (all smokers)	50–69	1985–1993	185 (CRC)	Fish	g/day verse <0.15 g/day ≥68 g/day verse <13 g/day	non-significant associations	Ref ([26])
JACC	45,181 men and 62,643 women	40–79	1988–1997	284 (Colon), 173 (Rectum)	Fish	everyday versus <2 days/week	non-significant associations	Ref ([36])
Ohsaki Cohort	18,858 men and 20,640 women	40–79	1995–2003	566 (CRC)	Fish	Men: ≥96.4 g/day verse <26.2 g/day Women: ≥81.4 g/day verse <26.6 g/day	non-significant associations	Ref ([37])
SMC	61,433 women	40–75	1987–2003	389 (Colon), 230 (Rectum)	Fish	≥2 servings/ week verse <0.5 servings/ week	non-significant associations	Ref ([28])
Oxford Vegetarian Study	4,162 men and 6,836 women	16–89	1980–1999	95 (CRC)	Fish	>one time/ week versus never	non-significant associations	Ref ([38])
NOWAC	63,914 women	40–70	1996–2004	254 (CRC)	Fish	>53.4 g/day verse <29.1 g/day	non-significant associations	Ref ([39])
Case-control	–	20–76	–	1,727 (Colon), 1,447 (Rectum), 5,039 (Control)	Fish	–	non-significant associations	Ref ([30])

Table 3

Characteristics of studies of fiber and CRC

Study	Number of study participants	Age of participants	Follow-up years	CRC incidence	Analytic category	Analytical comparison, high versus low intake	Relative risk (95% CI)	Ref
13 case-control studies	–	–	–	5,225 (CRC), 10,349 (Control)	Total fiber	>31.2 g/day versus <10.1 g/day	CRC: 0.53 (0.47–0.61), p<0.0001	Ref ([51])
16 case-control and 4 cohort studies	10,948 men and women	–	–	–	Total fiber	per 100g increase	CRC: 0.72 (0.63–0.83)	Ref ([53])
25 prospective studies	–	–	–	–	Total fiber	–	CRC: 0.90 (0.86–0.94)	Ref ([52])
EPIC	142,250 men and 335,062 women	35–70	1992–2002	2,869 (Colon), 1,266 (Rectum)	Total fiber	≥28.5 g/day versus <16.4 g/day	CRC: 0.83 (0.72–0.96), p=0.013	Ref ([56])
					Cereal fiber	≥12.3 g/day versus <4.64 g/day	CRC: 0.87 (0.77–0.99), p=0.003	
EPIC	131,985 men and 320,770 women	35–70	1992–2002	2, 819 (CRC)	Total fiber	–	CRC: 0.86 (0.75–1.00), p=0.04	Ref ([55])
PLCO	57,774 men and women	55–74	1993–2001	733 (CRC)	Total fiber	≥12.8 g/1000 kcal versus <9.9 g/ 1000 kcal	Distal colon cancer: 0.62 (0.41, 0.94), p=0.03	Ref ([57])
Case-control	–	30–75	–	341 (Colon), 265 (Rectum), 613 (Control)	Total fiber	Men: >14.92 g/day versus <7.73 g/day	CRC: 0.38 (0.27–0.55), p<0.01	Ref ([60])
						Women: >12.65 g/day versus <6.52 g/day		
JACC	16,636 men and 26,479 women	40–79	1988–1997	291 (Colon), 142 (Rectum)	Total fiber	–	CRC: 0.73 (0.51–1.03), p=0.028	Ref ([62])
NIH-AARP DHS	291,988 men and 197,623 women	50–71	1995–2000	2,974 (CRC)	Fiber from grains	>5.7 g/1000 kcal versus <1.7 g/ 1000 kcal	CRC: 0.86 (0.76–0.98), P=0.01	Ref ([65])
HELGA	38,841 men and 69,159 women	40–65	1991–2002	680 (Colon), 399 (Rectum)	Whole-grain wheat	Men: >9 g/day versus ≤1 g/day	CRC: 0.65 (0.50–0.84)	Ref ([66])
						Women: >36 g/day versus ≤3 g/day		

Study	Number of study participants	Age of participants	Follow-up years	CRC incidence	Analytic category	Analytical comparison, high versus low intake	Relative risk (95% CI)	Ref
13 prospective cohort studies	725,628 men and women	–	6 to 20 years	–	Total fiber	>30 g/day versus <10 g/day	non-significant associations	Ref ([54])
HPFS and NHS	47,279 men and 76,947 women	40–75/30–55	1986–2010/1980–2010	1,202 (Colon), 310 (Rectum)	Total fiber	>14 g/1000 kcal versus <8 g/1000 kcal	non-significant associations	Ref ([58])
WHS	36,976 women	45+	1993–2003	223 (CRC)	Total fiber	≥23.1 g/day versus <12.5 g/day	non-significant associations	Ref ([59])
SWHS	73,314 women	40–70	1997–2005	283 (CRC)	Total fiber	>13.45 g/day versus <7.3 g/day	non-significant associations	Ref ([61])
JPHC	65,803 men and 67,520 women	45–74	1995–2006	742 (Colon) and 375 (Rectum)	Total fiber	Men: >18.7 g/day versus <6.4 g/day Women: >20 g/day versus <8.3 g/day	non-significant associations	Ref ([63])
DCH	26,630 men and 29,189 women	50–64	1993–2009	461 (Colon), 283 (Rectum)	Total whole-grain	>160 g/dat versus ≤75 g/day	non-significant associations	Ref ([68])
NOWAC	78,254 women	40–70	1996–2006	509 (Colon), 218 (Rectum)	whole-grain bread	180–240 g/day versus 0	non-significant associations	Ref ([69])

Table 4

Characteristics of studies of fruit and vegetables and CRC

Study	Number of study participants	Age of participants	Follow-up years	CRC incidence	Analytic category	Analytical comparison, high versus low intake	Relative risk (95% CI)	Ref
EPIC	131,985 men and 320,770 women	35–70	1992–2006	2, 819 (CRC)	Fruit and vegetables	>603.6 g/day versus <221.1 g/day	CRC: 0.86 (0.75–1.00), p= 0.04	Ref ([55, 71])
NIH-AARP DHS	291,094 men and 196,949 women	50–71	1995–2000	2,972 (CRC)	Vegetables	Men: >2.8 servings/1000 kcal versus <0.6 servings/ 1000 kcal	Men-CRC: 0.82 (0.71–0.94), p=0.03	Ref ([74])
							Men-Distal colon cancer: 0.76 (0.59–0.98), p=0.04	
					Fruit	Women: >3.5 servings/ 1000 kcal versus <0.6 servings/1000 kcal	Women-Rectal cancer: 1.59(1.04–2.44), p=0.01	
					Green leafy vegetables	–	Men-CRC: 0.86 (0.74–0.99), p=0.04	
19 prospective studies	–	–	–	–	Fruit and vegetables	–	CRC: 0.92 (0.86 – 0.99)	Ref ([79])
24 case–control and 11 prospective studies	1,295,063 men and women		1978–2012	24,275 (CRC)	Cruciferous vegetable	–	CRC: 0.82 (0.75–0.90)	Ref ([81])
EPIC	477,312 men and women	35–70	1992–2006	2,869 (Colon), 1,648 (Rectrum)	Total flavonoids and flavonoid	–	non-significant associations	Ref ([72])
HPFS and NHS	42,478 men and 76,364 women	40–75/30–55	1986–2010/1980–2010	2,519 (CRC)	Flavonoid	–	non-significant associations	Ref ([73])
NLCS–MIC	58,279 men and 62,573 women	55–69	1986–2000	1,678 (Colon), 572 (Rectum)	Total flavonol and flavone	–	non-significant associations	Ref ([75])
Case-control	–	40–79	–	834 (CRC), 939 (Control)	Fruit and vegetables	>10.82 servings/day versus <5.77 servings/day	non-significant associations	Ref ([77])
6 cohorts and 11 case–control	–	–	–	–	Fruit and vegetables	–	non-significant associations	Ref ([78])
14 cohort studies	756,217 men and women	–	6 to 20 years	5,383 (Colon)	Fruit and vegetables	–	non-significant associations	Ref ([80])
6 cohorts	686,629 men and women	–	–	4,062 (CRC)	Semi-vegetarian diet	Versus non-vegetarian diet	CRC: 0.86 (0.79–0.94)	Ref ([83])
					Pesco-vegetarian diet	Versus non-vegetarian diet	CRC: 0.67 (0.53–0.83)	

Study	Number of study participants	Age of participants	Follow-up years	CRC incidence	Analytic category	Analytical comparison, high versus low intake	Relative risk (95% CI)	Ref
AHS II	77,659 men and women	–	2002–2009	380 (Colon), 110 (Rectum)	Vegetarian diet	Versus non-vegetarian diet	CRC: 0.78 (0.64-0.95), p=0.01	Ref [82]
					Pesco-vegetarian diet	Versus non-vegetarian diet	CRC: 0.57 (0.40–0.82), p=0.002	
EPIC-Oxford	12,230 men and 40,476 women	20–89	1993–2005	290 (CRC)	Vegetarian	Versus non-vegetarian	CRC: 1.49 (1.09–2.03)	Ref [84]
					Vegetarian or vegan	Versus meat-eater	CRC: 1.39 (1.01–1.91)	

Table 5

Characteristics of studies of vitamins and minerals and CRC

Study	Number of study participants	Age of participants	Follow-up years	CRC incidence	Analytic category	Analytical comparison, high versus low intake	Relative risk (95% CI)	Ref
Case-control	–	–	–	1,723 (Colon), 3,097 (Control)	Multiple vitamins	>5 years versus nerver or <1 year	Women-Colon cancer: 0.7 (0.4–1.3), p=0.03	Ref ([85])
					B-complex vitamins		Women-Colon cancer: 0.4 (0.2–0.7), p=0.0005	
					Vitamin E		Women-Colon cancer: 0.6 (0.4–0.9), p=0.002	
					Calcium		Women-Colon cancer: 0.4 (0.3–0.6), p<0.0001	
					Iron		Women-Colon cancer: 0.6 (0.4–1.0), p=0.03	
					Zinc		Women-Colon cancer: 0.4 (0.2–0.9), p=0.03	
Case-control	–	–	–	2,349 (CRC), 4,168 (Control)	Vitamin B6	>5 mg/day versus <1 mg/day	Women-Rectal cancer: 3.57 (1.56–8.17), p=0.01	Ref ([88])
DCH	56,332 men and women	50–64	1993–2009	465 (Colon), 283 (Rectum)	Dietary folate	–	CRC: 0.83 (0.57–1.21), p=0.04	Ref ([89])
					Supplemental folate	–	CRC: 0.83(0.58–1.20), p=0.76	