Supplementary Table 1. Components with a protective effect on CRC prevention

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
			ASPIRIN				
Bosetti et al., 2006 Italy [10]	up to December 2005 Medline	**Inclusion:** not specific other than search sting terms **Exclusion:** Articles reporting estimates for all NSAIDs combined	Aspirin	NS	CRC incidence 11 case-control; 7 Cohort	Overall**:** **RR=0.71 (0.67;0.75)** case-control: **RR=0.59 (0.54;0.64)** Cohort: **RR=0.85 (0.78;0.92)**	Quality score and publication bias: not performed Heterogeneity: <0.001
Dubé et al., 2007 Canada [14]	up to December 2006 Medline, preMedline, Embase and Central	**Inclusions:** Patients at average risk of CRC **Exclusions:** 1) studies of familial adenomatous polyposis or hereditary nonpolyposis colon cancer syndromes (Lynch I or II); 2) Secondary prevention studies of patients with a history of CRC	Aspirin regular use	NS	CRC incidence 2 RCT; 7 case-control; 6 Cohort	case-control: 1 to 3 years: **RR=0.85 (0.72;1.00)** 4 to 6 years **RR=0.74 (0.60;0.90)** Cohort: **RR=0.78 (0.63;0.97)**	Quality score; heterogeneity; publication bias: NS
			Low dose aspirin (100-325 mg/day)	Placebo	CRC incidence 2 RCT	RR=1.02 (0.84; 1.25)	Quality score; heterogeneity; publication bias: not specified.
Din et al., 2010 UK [11]	From 1980 to 2010 Medline and ISI web of knowledge	**Inclusions:** (1) studies measuring CRC incidence; (2) the strength of association had to be stated in the form of RR or OR; and (3) the study population had to be comparable with the general population; **Exclusions:** Not English article	Low dose aspirin: ≤ 165 mg daily	NS	CRC incidence 6 case-control; 4 Cohort	<u>Dose response:</u> <525mg/week: **RR= 0.79 (0.66;0.95)** 525;1050 mg/week: RR=0.69 (0.43;1.11) >1050 mg/week: RR=0.73 (0.33;1.60) case-control: OR=0.81 (0.63;1.04) Cohort: RR =0.90 (0.90, 1.09) case-control: OR=0.81 (0.63; 1.04)	Quality score; publication bias: not specified. Heterogeneity case-control: p=0.06 Cohort: p=0.44

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
						Cohort: RR =0.90 (0.90, 1.09)	
			Low dose aspirin: ≤ 165 mg daily	NS	CRC incidence 6 case-control; 4 Cohort	75mg/day **RR= 0.78 (0.65;0.92)** <525mg/week: **RR=0.79 (0.66;0.95)** Duration: 75mg/day for: 0-1 year RR=0.87 (0.59;1.28), 5-10 years: **RR=0.63 (0.45;0.87)** >10 years RR=0.82 (0.58;1.16). case-control: OR=0.81 (0.63; 1.04) Cohort: RR =0.99 (0.90, 1.09)	
Bosetti et al., 2012 Italy [12]	Up to September 2011 Pubmed and Medline	**Inclusions:** 1) aspirin use considered separately from other NSAIDs; 2) original data 3) not based on selected patients with specific diseases; 4) published in English language; **Exclusions:** 1) patients with rheumatoid arthritis; 2) study on users on low;dose aspirin only 3) RCT of aspirin, usually with cardiovascular events as the primary endpoint; 4) multiple reports were published on the same population or subpopulation (included only the most recent and the informative one)	Aspirin; Regular aspirin use at least 1–2 tablets per week) or alternatively ever/any use	NS	**CRC incidence** 15 case-control; 15 Cohort 37,519 cases (21,414 from case-control and 16,105 from Cohort)	**RR=0.63 (0.56–0.70)** **Cohort** **RR=0.82 (0.75–0.89)** <u>Daily Aspirin use</u> **RR=0.66 (0.57–0.77)** <5 years **RR=0.80 (0.71–0.91)** >5 years **RR=0.75 (0.70–0.80)** <u>Low dose</u> RR=0.95 (0.76–1.19) <u>High dose</u> **RR=0.69 (0.57–0.85)**	Quality score: not performed Heterogeneity: Overall <0.001 (I^2=75.5%) case-control <0.001 (I^2=65.4%) Cohort<0.001 (I2=66%) Duration p=0.369 Publication bias: yes
					Colon	Overall	Not reported

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
					cancer incidence 6 case-control; 6 Cohort	**RR=0.71 (0.63;0.80)** case-control: **RR=0.61 (0.50–0.76)** Cohort: **RR=0.77 (0.67–0.89)**	
					Rectal cancer incidence 3 case-control; 6 Cohort	**RR=0.68 (0.55;0.83)**	Not reported
Yé et al., 2013[13] China	January 1990 to June 2012 Medline, Pubmed, Embase, ISI web, web of science, wanfang and cnki	**Inclusions:** 1) Cohort study design; 2) provide information on aspirin use in relation to CRC; 3) include three or more quantitatively measured exposure categories of aspirin use (such as dose, frequency and duration); 4) have CRC incidence as defined above as the endpoint; and 5) report original data and include HR or RR and their 95% CIs **Exclusion:** 1) not published as full reports 2) cross-sectional or case-control design; 3) based on selected patients with specific diseases (such as adenomas, ulcerative colitis or prior cancer) 4) When multiple reports were published on the same population or subpopulation, only the most recent and informative one were selected	Aspirin highest Dose	Aspirin lowest Dose	**CRC incidence** 5 Cohort	Overall: **RR=0.74 (0.64;0.83)**	Quality score; not performed Heterogeneity: p=0.545 (I^2=0.0%) Publication bias: No
			Aspirin highest Frequency	Aspirin lowest Frequency	**CRC incidence** 9 Cohort	**RR=0.80 (0.75;0.85)** <u>Subgroup:</u> Men: **RR=0.60 (0.27;0.93)** Women: **RR=0.82 (0.73;0.91)** Colon: **RR=0.76 (0.65;0.87)** Rectal: **RR=0.74 (0.64;0.83)**	Quality score; not performed Heterogeneity: p=0.384 (I^2=6.2%) Publication bias: Slight
			Aspirin highest Duration	Aspirin lowest Duration	**CRC incidence** 9 Cohort	**RR=0.75 (0.68;0.81)** <u>Subgroup:</u> Men: **RR=0.70 (0.54;0.86)** Women: **RR=0.73 (0.62;0.84)**	Quality score; not performed Heterogeneity: p=0.160 (I^2=31.1%) Publication bias: Yes

Study Country (Reference)	**Search period and databases searched**	**Inclusion / exclusion criteria**	**Intervention**	**Control**	**Outcomes**	**Results**	**Quality score Heterogeneity Publication bias**
						Colon: **RR=0.67 (0.44;0.91)** Rectal: **RR=0.54 (0.20;0.88)**	
			Dose response	Vs no intake		75 mg/day **RR=0.90 (0.86;0.94)** 163 mg/day **RR=0.86 (0.81;0.91)** 325 mg/day **RR=0.80 (0.74;0.88)**	Quality: not performed Heterogeneity: unknown Publication bias: no
Emilsson et al, 2017 Norway [15]	Up to 31 October 2015 COCHRANE central register Medline and EMBASE	**Inclusion**: RCT reporting CRC mortality, CRC incidence, or both, with a minimum FU of 2 years and more than 100 included individuals **Exclusions:** high;risk populations (such as individuals with familial adenomatous polyposis or Lynch syndrome)	Aspirin	Placebo	**CRC incidence** 6 RCT	**Colorectal RR=0.86 (0.76;0.98) Proximal: RR=0.58 (0.46;0.74) Distal:** RR=0.77 (0.58;1.04)	Quality score; no quality score Heterogeneity: Colorectal: I^2= 22.6% Publication bias: unknown
NSAID							
Rostom et al., 2007 Canada [16]	up to December 2006 MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), and Cochrane Library	**Inclusions:** 1) subjects at average risk for CRC (that is, no known risk factors for colorectal adenoma or CRC, other than age) 2) studies of higher;risk individuals with a personal or family history of CRA or a family history of sporadic CRC 3) addressed the incidence of CRA, CRC, or both and CRC related death or overall death. **Exclusions:** 1) studies of high risk patients with familial adenomatous polyposis or hereditary nonpolyposis colon cancer syndromes (Lynch I or II) and secondary	Regular use of non-ASA NSAIDs for ≥ 1 year	NS	CRC incidence 4 case-control; 3 Cohort	**case-control: RR=0.70(0.63;0.78) Cohort: RR=0.61(0.48;0.77)**	Not reported
			Regular use of any NSAID for ≥ 1 year	NS	3 Cohort	**RR=0.57(0.47;0.68)**	Not reported

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
		prevention studies of patients with a personal history of CRC.					
Din et al., 2010 UK [11]	From 1980 to 2010 Medline and ISI web of knowledge	**Inclusions:** (1) studies that measured CRC incidence; (2) the strength of association had to be stated in the form of RR or OR; and (3) the study population had to be comparable with the general population; **Exclusions:** Not English article	NSAID	NS	CRC incidence 6 case-control; 4 Cohort	Any NSAID **RR=0.73 (0.64;0.83)** Non-aspirin NSAID **RR= 0.74 (0.60;0.90).** Duration: Any NSAID 0-1 year: RR= 0.82 (0.66;1.03) 5-10 years: **RR= 0.57 (0.44;0.75)**	Quality score; publication bias: not specified. Heterogeneity NS
Tomic et al., 2018 [17]	From 1985 to April 2019	**Inclusions:** (1) original clinical studies; (2) studies that included participants aged 40 years or older, male and/or female; (3) exposure- NA-NSAIDs; (4) case-control, Cohort or RCT studies providing information about association measures- OR, RR and their CI analysing the effects of NA-NSAIDs on CRC risk or providing sufficient data from which it could be calculated; and studies written in English, French, Spanish, German or Italian **Exclusions:** (1) preclinical studies; (2) studies including participants of all ages; (3) exposure- Aspirin included; (4) studies based solely on mortality/survival rates; (5) secondary prevention studies, where the main aim has not been the investigation of the NA-NSAIDs effect on CRC prevention; and finally (6) reviews, previous meta-analysis, editorials or letters			CRC incidence 10 Cohort, 13 case-control, Higher dose 5 Cohort Lower doses 3 case-control	Combined analysis: **OR=0.74 (0.67;0.81)** (random effect) Cohort: **OR=0.80 (0.72;0.88)** case-control: **OR = 0.61 (0.50;0.75)** Men overall: OR=0.86 (0.70;1.06) Men case-control OR=0.80 (0.58;1.12) Women overall: **OR=0.67 (0.53;0.85)** Women Cohort **OR=0.81 (0.67;0.98)** Higher doses **RR= 0.82 (0.69;0.99)** Lower doses RR= 0.92 (0.83;1.01) Proximal colon cancer **RR=0.73 (0.60;0.87)**	**Quality score** NOS **Heterogeneity** Combined analysis I^2 = 75.9%, p < 0.001 Cohort; I^2 = 69.9%, p < 0.001 case-control: I^2 =80.1%, p < 0.001 Men overall : I^2 =15.9% p=0.312, Women overall I^2=54.5% p=0.031 Higher doses I^2=0%, p=0.594 Lower doses I^2=0.9%, p=0.365 Proximal colon cancer I^2=63.8, p=0.017 Distal colon cancer

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
						Distal colon cancer **RR=0.78 (0.69;0.88)** Rectal cancer RR= 0.82 (0.67;1.01) Duration > 5 years **RR = 0.80 (0.68;0.94)**	I^2=0%, p= 0.17 Rectal cancer I^2=51%, p=0.057 Duration > 5 years I^2 = 0%, p < 0.465 **Publication biases** Egger's test Overall p = 0.006 case-control p = 0.001 Cohort p = 0.809
MAGNESIUM							
Chen et al. 2012 China [19]	Until July 2012 Pubmed	**Inclusions:** 1) case-control and Cohort, 2) exposure was intake of dietary Mg or total Mg (dietary and supplements combined), 3) outcome was colorectal, colon or rectal cancer and, 4) RR estimates OR in nested case–control studies with corresponding 95% CI provided, or could be calculated using the raw data presented in the studies **Exclusions:** 1) Non prospective design	Magnesium intake* highest category	Mg intake lowest category	CRC risk 1CC; 7 Cohort N=338,979 for case-control and Cohort	Overall: RR=0.89 (0.79;1.00) **Cohort: RR=0.87 (0.77;0.99)** Dose-response analysis increment of 50 mg/day CRC RR=0.95(0.89;1.00) Colon cancer **RR=0.93(0.88;0.99**) Rectal cancer RR=0.93(0.83;1.04)	Quality not reported Heterogeneity: Overall: I^2= 0%, p = 0.46 Cohort: I^2= 0%, p = 0.43 Publication bias: no indication of publication bias
Wark et al. 2012 Netherlands [18]	1966-31 July 2011 Pubmed	**Inclusions:** 1) presented RR estimates and their variances or sufficient data to obtain these effect measures, 2) if multiple publications presented findings on the same study population, only the most recent information was used	Magnesium intake* highest category	Magnesium intake lowest category	CRC risk 6 Cohort N=252,867 for Cohort	RR = 0.85 (0.71; 1.00) Random-effects model **RR = 0.84 (0.73; 0.97)** fixed-effects models NB: Dose response effect RR= 0.87 (0.75;	Quality not reported Heterogeneity: Overall: I^2= 27%, p = 0.23 Publication bias:

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
						1.01) per 100 mg/d	no indication of publication bias
Ko et al., 2014 Korea [20]	Up to November 2012 PubMed, Cochrane Library, and SCOPUS	**Inclusions:** 1) case-control or Cohort studies on the relationship between magnesium intakes and cancer, 2) human; 3) dietary magnesium; and 4) cancer incidence regardless of cancer types. **Exclusions:** 1) supplementary magnesium or with magnesium from drinking water, 2) in vitro 3) mortality, and 4) review articles, letters, and case reports.	Magnesium intake* highest category	Mg intake lowest category	CRC risk** 4 Cohort and case-control N=1,236,004 for case-control and Cohort for all cancer outcomes (unk for colorectal)	**RR = 0.78 (0.66; 0.92)** fixed-effects models	Yes, using the NOS, mean of NOS was 5.7 stars in case-control studies and 7.4 starts in cohort studies. Based on this data, we decided the NOS cut-off for a high-quality study to be ≥6 stars for case-control study and ≥8 stars for cohort studies. 4 high-quality case-control studies and 5 high-quality prospective cohort studies Heterogeneity: Overall: I^2= 17% Publication bias: Publication for overall cancer (unk for colorectal) Heterogeneity: Overall: I^2= 17% Publication bias: for overall cancer (unk for colorectal)
FOLIC ACID							

Study Country (Reference)	**Search period and databases searched**	**Inclusion / exclusion criteria**	**Intervention**	**Control**	**Outcomes**	**Results**	**Quality score Heterogeneity Publication bias**
Kennedy et al., 2011 Canada [21]	up to October 2009 MEDLINE, Embase and Scopus	**Inclusions:** 1) observational studies, 2) folate exposure (dietary or total) 3) at least two levels of folate intake, 4) association with rates of colorectal, colon and/or rectal cancer. **Exclusions:** 1) no clear levels of folic acid intake.	High Folate intake (dietary or total) [1] Cohort : FU 8-22years case-control: 1-2 year before diag	Low folate intake	CRC incidence 18 case-control 9 Cohort	Total folate **Cohort: RR=0.85(0.74;0.99)** Dietary folate case-control: RR=0.87(0.74;1.02) Cohort: RR=0.92(0.81;1.05) Rectal cancer only: case-control: RR=0.89(0.64;1.25) Colon cancer only case-control: RR=1.03(0.88;1.20) **Cohort: RR=0.75(0.57;0.99)** Men only: case-control: RR=0.89(0.66;1.19)	Quality performed: Downs and Black scoring tool Heterogeneity: Total folate I^2 = 11%; p = 0.34, Publication bias: some publication bias
Heine-Bröring et al., 2015 [22]	Up to January 2013 Medline, Embase and Cochrane	**Inclusions:** prospective Cohort studies if they reported original and peer-reviewed data on the association of dietary supplement use and colorectal, colon, or rectal cancer incidence. To be included in the meta-analyses, information on ascertainment of CRC cases, and estimates of the RR with 95% CI were required **Exclusions:** studies on colorectal adenomas, RCTs and case-control	Highest level of folate intake FU : 8-24yrs	Lowest level of folate intake	CRC incidence 3 Cohort	**RR=0.88(0.78;0.98)**	Quality performed: none Heterogeneity: I^2=6%; p=0.34 Publication bias: not reported

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
Liu et al., 2015 China [23]	Up to April 2014 Pubmed	**Inclusions**: [1] Cohort studies [2];the exposure of interest was vitamin or multiple-vitamin supplement intake [3] the outcome of interest was the incidence of colorectal, colon, or rectal cancer [4] relative risk (RR) or OR estimates with 95 % CI were reported. **Exclusions:** Articles with<6 stars.	Highest level of Folate intake	Lowest level of Folate intake	**CRC incidence** 19 Cohort	**RR=0.88(0.81;0.95)** Random effect model	Quality performed: NOS 8-6 stars Heterogeneity: I^2=43%, p=0.02 Publication bias: p=0.08
FOLIC ACID In Combination							
Carroll et al., 2010 UK [24]	Up to June 2008 Cochrane Library, MEDLINE, PreMEDLINE, CINAHL, EMBASE, Web of Science, BIOSIS and Research Registers	**Inclusions:** 1) RCTs, 2) folic acid or folate, 3) with or without other agents, **Population:** No increased risk CRC 3 studies (for CRC incidence)	Folic Acid + Vit B vitamins ± antioxidants	Placebo ± antioxidants	CRC incidence* 3 RCT N=11,062	RR=1.13(0.77; 1.64) Random effect model	Quality performed with a published scale Heterogeneity: Overall: I^2 = 7%, p=0.34 Publication bias: unk for CRC
Wien et al. 2012 Norway [26]	Up to March 2010 (May 2010/31 January 2011) (non-systematic) Cochrane Library, Medline, Embase	**Inclusions:** 1) RCTs, case-control or Cohort, 2) assessed cancer incidence and/or cancer mortality, 3) any population taking folic acid supplements ≥0.4 mg/day by oral route for any indication **Exclusions:** 1) folic acid given as part of high-dose cytostatic regimen of cancer treatment. **Population:** Seven RCTs were performed in populations with	Folic acid ≥ 0.4mg/day ± other Vit	Any control	CRC incidence* 9 RCT 1 Cohort 10 RCTs reporting overall cancer incidence N=38 233 (unk for	RCT: RR=1.00(0.83; 1.21) Cohort: RR=0.45(0.05; 3.92)	Quality performed: yes Heterogeneity: I^2 = 0%; (unk for CRC) Publication bias: No indication based on forest plots (unk for CRC)

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
	and Centre of Reviews and Dissemination, clinical trial registries	cardiovascular disease or high-risk groups for cardiovascular disease, three were in populations with a history of colorectal adenoma, one in a population with atrophic gastritis and one was performed in pregnant women.			CRC)		
Qin et al. 2015 China [25]	up to October 2014 Pubmed and Embase	**Inclusions:** 1) RCT, 2) correlation between folic acid supplementation and colorectal cancer risk, 3) RR with a 95% CI or the number of colorectal cancer events was reported; 4) the supplementary folic acid level was stated; 5) published in English. **Population:** Vascular disease, diabetes, CR adenoma, cardiovascular disease, stroke, transient ischemic attack, general	Folic acid supplementation 0.5mg to 2.5mg/day ± vit B6, B12, Aspirin	placebo	CRC incidence 8 RCTs N= 34,598	RR=1.00(0.82; 1.22) Male only: RR=1.01(0.82; 1.23)	Quality performed: yes Heterogeneity: I^2 = 0%; p = 0.82, Publication bias: Egger=0.33
DAIRY PRODUCTS							
Aune et al., 2012 UK [28]	Up to May2010	**Inclusions:** 1) Cohort or case-control, 2) total dairy products or specific types of dairy products and colorectal cancer incidence	High total diary product	Low total diary product	CRC Risk 12 Cohort 1,170,942 participants 11,579 cases	**RR=0.81(0.74;0.90)** Dose response 400 g increase per day (g/day) **RR=0.83(0.78;0.88**)	Quality not reported **Heterogeneity:** p=0.06; I^2=42% **Publication bias:** Egger p=0.58 Begg p=0.79
					Colon 5 Cohort	RR= 0.72(0.51;1.02) Dose response 400 g increase per day (g/day) **RR=0.84(0.72;0.97**)	**Heterogeneity:** p=0.09; I^2=50%
					Rectal 5 Cohort	RR=0.96(0.65;1.41) Dose response 400 g increase per day (g/day)	**Heterogeneity:** p=0.13; I^2=44%

Study Country (Reference)	**Search period and databases searched**	**Inclusion / exclusion criteria**	**Intervention**	**Control**	**Outcomes**	**Results**	**Quality score Heterogeneity Publication bias**
						RR=1.00(0.77;1.28)	
			Milk high consumption	Milk low consumption	CRC 10 Cohort 655,483 participants 5,011 cases	**RR=0.83(0.74;0.93)** Dose response 200 g increase per day (g/day) **RR=0.90(0.85;0.94)**	Quality not reported **Heterogeneity:** p=0.31; I^2=14% **Publication bias:** Egger p=0.86 Begg p=0.84
					Colon 4 Cohort	**RR=0.82(0.72;0.94)** Dose response 200 g increase per day (g/day) **RR=0.88(0.79;0.97)**	**Heterogeneity:** p=0.54; I^2=0%
					Rectal 4 Cohort	RR=0.79(0.60;1.06) Dose response 200 g increase per day (g/day) RR=0.90(0.79;1.02)	**Heterogeneity:** p=0.79; I^2=0%
			Cheese high consumption	Cheese low consumption	**CRC Risk** **177,551 participants** **1,635 cases** **7Co**	RR=0.94(0.75;1.18) Dose response 50 g increase per day (g/day) RR=0.96(0.83;1.12)	Quality not reported **Heterogeneity:** p=0.14; I^2=39% **Publication bias:** Egger p=0.86 Begg p=0.84
					Colon **5 Cohort**	RR=1.04(0.69;1.55) Dose response 50 g increase per day (g/day) RR=0.84(0.68;1.04)	**Heterogeneity:** **p=0.05; I^2=58%**
					Rectal **3 Cohort**	RR=0.88(0.59;1.30) Dose response 50 g	**Heterogeneity:** p=0.84; I^2=0%

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
						increase per day (g/day) RR=0.90(0.70;1.15)	
Ralston et al., 2014 Australia [29]	January 2002 to July 2009	**Inclusion**: 1) English language, 2) human population, 3) keywords relating only to dairy and CRC **Exclusion**: 1) calcium or vitamin D intake rather than dairy food intake, or 2) examined total dairy food intake rather than specific types of dairy foods.	Highest category (ranged from >35 to >976 g non-fermented milk/day, >8 to >70 g solid cheese/day, and >110 to >350 g fermented milk/day)	Lowest category (ranged from 0 to <407, <2.5 to <30, and 0 to <32 g/day for non-fermented milk, solid cheese, and fermented milk)	CRC risk 15 Cohort 919,680 subjects, 5,200 cases	Non fermented milk overall : **RR=0.85(0.77; 0.93)** (in the highest category of intake average: 439 g non fermented milk/day). Subgroup: CRC men **RR=0.79(0.69; 0.91)**, CRC women RR=0.83(0.68;1.02) Solid cheese overall RR=1.11 (0.90; 1.36) Subgroup: CRC men RR=0.94 (0.58; 1.54) CRC Women RR=1.16 (0.82;1.63) Fermented milk overall RR=1.01 (0.89; 1.15), Subgroup: CRC men RR=1.08 (0.90; 1.29) CRC women RR=0.93 (0.87; 1.12)	**Individual quality performed** **Heterogeneity:** Non fermented milk overall CRC: I^2 =0% <u>Men</u> CRC 0% colon I^2=0%, rectal I^2=0%, <u>Women</u> CRC 42% Colon I^2=0%, rectal I^2=0%, Solid Cheese CRC I^2=16% solid cheese CRC men 43%, solid cheese CRC Women 11% Fermented milk overall 0% men I^2=0% women 0%
					Colon	Non Fermented milk men: **RR=0.74 (0.60; 0.91)** women :	

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
						RR=1.03 (0.78; 1.36),	
					Rectal	Non fermented milk men: RR=0.81 (0.60; 1.09) women: RR=0.82 (0.56; 1.21),	
Vieira et al, 2017* **UK** [27]	**Up to May 2015**	**Inclusion:** 1) RCT, Cohort or case-control design, 2) report adjusted estimates of the RR and 95% CIs for the association of foods and CRC incidence; 3) for dose-response meta-analysis, studies should provide a quantitative measure of the intake.	Total diary product Dose response Incremental of 400 g/day		**CRC** 10 Cohort or case-control	**RR=0.87 (0.83; 0.90)**	High quality studies but not detailed **Heterogeneity:** p=0.14; I^2=18% **Publication bias:** none detected
					Colon 6 Cohort or case-control	**RR=0.87 (0.81; 0.94)**	High quality studies but not detailed **Heterogeneity:** p=0.25; I^2=24% **Publication bias:** none detected
					Rectal **5 Cohort or case-control**	RR= 0.93 (0.82; 1.06)	High quality studies but not detailed **Heterogeneity:** NS **Publication bias:** none detected
			Milk product Dose response Incremental of 200 g/day		**CRC** 9 Cohort or case-control	**RR= 0.94 (0.92; 0.96)**	High quality studies but not detailed **Heterogeneity:** p=0.97; I^2=0%

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
							Publication bias: none detected
					Colon 9 Cohort or case-control	**RR= 0.93 (0.90; 0.96)**	High quality studies but not detailed **Heterogeneity:** p=0.18; I^2=30% **Publication bias:** none detected
					Rectal 7 Cohort or case-control	**RR= 0.94 (0.91; 0.97)**	High quality studies but not detailed **Heterogeneity:** p=0.93; I^2=0% **Publication bias:** none detected
			Cheese product Dose response Incremental of 50 g/day		**CRC** 9 Cohort or case-control	RR=0.94 (0.87; 1.02)	High quality studies but not detailed **Heterogeneity:** NS **Publication bias:** none detected
					Colon 9 Cohort or case-control	RR=0.91 (0.80; 1.03)	
					Rectal 4 Cohort or case-control	RR=0.95 (0.90; 1.00)	
FIBER							
Trock et al., 1990 USA [31]	1970 up to 1988	**Inclusions:** All epidemiologic studies concerning CRC and fiber, vegetables, grains, or fruit published in English	High intake total dietary fiber (varying cut-off)	Low intake total dietary fiber (varying cut-off)	**CRC risk** 10CC	Combined **OR=0.57 (0.50; 0.64)** Fiber: **OR=0.58 (0.51; 0.66)**	Quality not reported **Heterogeneity:** p<0.01

Study Country (Reference)	**Search period and databases searched**	**Inclusion / exclusion criteria**	**Intervention**	**Control**	**Outcomes**	**Results**	**Quality score Heterogeneity Publication bias**
Haas et al., 2009 Brazil [32]	1950 up to December 2006	**Inclusions:** epidemiological studies of cohorts that evaluated the effectiveness of whole grains in the prevention of CRC by means of questionnaires on feed frequency	High intake total dietary fiber (varying cut-off)	Low intake total dietary fiber (varying cut-off)	**CRC risk** 10 Cohort 7,745 cases 1,719,590 patients	Highest quintile: RR= 0.94 (0.85; 1.03) Lowest quintile RR=0.96 (0.88; 1.04)	Quality not reported **Heterogeneity not reported**
Aunes et al., 2011 UK [30]	Up to December 2010	**Inclusions:** 1) Cohort or case-control, 2) investigate the association between dietary fiber or whole grain intake and incidence of colorectal cancer	High intake total dietary fiber	Low intake total dietary fiber	CRC Risk 19 Cohort or case-control	**RR=0.88 (0.82; 0.94)** Dose response analysis 10 g/day intake **RR=0.90 (0.86; 0.94)**	Quality not reported **Heterogeneity:** p=0.48; I^2=0% No publication bias
			Fruit fiber high intake	Fruit fiber low intake	CRC risk 9 Cohort	RR= 0.94 (0.85; 1.04) Dose response analysis 10 g/day intake RR=0.93 (0.82; 1.05)	Quality not reported **Heterogeneity:** p=0.11; I^2=39% No publication bias
			Vegetable fiber high intake	Vegetable fiber low intake	CRC risk 9 Cohort	RR= 0.98 (0.91; 1.06) Dose response analysis 10 g/day intake RR=0.98 (0.91; 1.06)	Quality not reported **Heterogeneity:** p=0.48; I^2=0% No publication bias
			Legume fiber high intake	Legume fiber low intake	CRC risk 4 Cohort	RR= 0.89 (0.78; 1.02) Dose response analysis 10 g/day intake RR=0.62 (0.27; 1.42)	Quality not reported **Heterogeneity:** p=0.17; I^2=41% No publication bias
			Cereal fiber high intake	Cereal fiber low intake	CRC risk 8 Cohort	**RR= 0.90 (0.83; 0.96)** Dose response analysis 10 g/day intake RR=0.62 (0.27; 1.42)	Quality not reported **Heterogeneity:** p=0.94; I^2=0% No publication bias

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
			Whole grain high intake	Whole grain low intake	CRC risk 7 Cohort	**RR= 0.79 (0.72; 0.86))** Dose response analysis 90 g/day (3 servings) intake **RR=0.83 (0.78; 0.89)**	Quality not reported **Heterogeneity:** p=0.98; I^2=0% No publication bias
Vieira et al, 2017* UK [27]	**Up to May 2015**	**Inclusion:** 1) RCT, Cohort or case-control design, 2) report adjusted estimates of the RR and 95% CIs for the association of foods and CRC incidence; 3) for dose–response meta-analysis, studies should provide a quantitative measure of the intake.	Whole grains Dose response Incremental of 90g/day		CRC risk 6 Cohort	**RR= 0.83 (0.79; 0.89)**	Quality not reported **Heterogeneity:** p=0.30; I^2=18% No publication bias
					Colon 4 Cohort	**RR=0.82 (0.73; 0.92)**	**Heterogeneity:** p=0.49; I^2=0%
					Rectal 3 Cohort	RR=0.81 (0.54; 1.20)	**Heterogeneity:** P<0.01; I^2=91%
Gianfredi et al., 2018 Italy [33]	Up to October 2016 Pubmed	**Inclusions :** 1) articles in English only; 2) full text articles; 3) performed on humans; 4) focussed on fibre intake; 5) epidemiological studies evaluating the relationship between fibre intake and risk of colon cancer alone. **Exclusions:** 1) all the studies evaluating colon and rectal cancer in combination 2) different outcome; 3) studies without proper sufficient statistics 4) in vitro model studies; 5) animal model studies; 6) experimental animal models; 7) studies without original data	High intake total dietary fiber (varying cut-off)	Low intake total dietary fiber (varying cut-off)	Colon 25 case-control or Cohort N=2,627,391	**RR=0.74 (0.67; 0.82)** Subgroup Female: RR=0.88 (0.73; 1.05), Male: RR=0.92 (0.81; 1.04)	**Heterogeneity:** P=0.01; I^2=44% No publication bias
FRUIT AND VEGETABLE							
Trock et al., 1990 USA [31]	1970 up to 1988	**Inclusions:** All epidemiologic studies concerning CRC and fiber, vegetables, grains, or fruit published in English	High intake total vegetable	Low intake total vegetable	**CRC risk** 10CC	Vegetable **OR=0.48 (0.41; 0.57)**	Quality not reported **Heterogeneity:** p<0.01

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
Huxley et al., 2009* Australia [34]	1996 to January 2008	**Inclusions:** 1) published quantitative estimates and standard errors (or some other measure of variability) of the association between each risk factor and 2) CRC **Exclusions:** 1) provided only an estimate of effect, with no means by which to calculate the standard error, or if the estimates were not at least age adjusted	High intake total fruit	Low intake total fruit	CRC Risk 16 Cohort	RR=0.99 (0.90; 1.08)	Quality not reported **Heterogeneity:** p=0.11 Publication bias: Egger p=0.30
					Colon	RR=1.01 (0.86; 1.18)	-
					Rectal	**RR=0.78 (0.63; 0.97)**	**Heterogeneity:** p=0.06
			High intake vegetable	Low intake vegetable	CRC Risk 16 Cohort	RR=0.95 (0.88; 1.04)	Quality not reported **Heterogeneity:** p=0.18 Publication bias: Egger p=0.29
					Colon	RR=0.93 (0.85; 1.10)	-
					Rectal	RR=0.88 (0.69; 1.12)	-
Aune et al., 2011 UK [35]	Up to May 2010	**Inclusions:** 1) Cohort or case-control, 2) fruit and vegetable intake and colorectal cancer risk.	High intake total fruit and vegetable combined	Low intake total fruit and vegetable combined	CRC Risk 11 Cohort 1,523,860 participants 11,853 cases	**RR=0.92 (0.86; 0.99)** Dose response analysis 100 g/day intake **RR=0.98 (0.97; 0.99)**	Quality not reported **Heterogeneity:** p=0.24; I^2=22% Publication bias: Egger p=0.52
					Colon 12 Cohort	**RR=0.91 (0.84; 0.99)**	Quality not reported **Heterogeneity:** p=0.32; I^2=13%
					Rectal 10 Cohort	RR= 0.97 (0.86; 1.09)	Quality not reported **Heterogeneity:** p=0.65; I^2=0%
			High intake	Low intake	CRC Risk	**RR= 0.90 (0.83; 0.98)**	Quality not reported

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
			total fruit	total fruit	14 Cohort	Dose response analysis 100 g/day intake **RR=0.89 (0.81; 0.98)**	**Heterogeneity:** p=0.05; I^2=42% Publication bias: Egger p=0.79
					Colon 11 Cohort	**RR=0.89 (0.81; 0.98)**	Quality not reported **Heterogeneity:** p=0.14; I^2=33%
					Rectal 7 Cohort	RR=0.91 (0.76–1.09)	Quality not reported **Heterogeneity:** p=0.09; I^2=45%
			High intake total vegetable	Low intake total vegetable	CRC 15 Cohort	**RR=0.91 (0.86–0.96)** Dose response analysis 100 g/day intake **RR=0.90 (0.85; 0.95)**	Quality not reported **Heterogeneity:** p=0.53; I^2=0% Publication bias: Egger p=0.14
					Colon 11 Cohort	**RR=0.87 (0.81; 0.94)**	Quality not reported **Heterogeneity:** p=0.70; I^2=0%
					Rectal 8 Cohort	RR=0.94 (0.85; 1.04)	Quality not reported **Heterogeneity:** p=0.59; I^2=0%
Wu et al., 2013 China [36]	**Up to April 2012**	**Inclusions:** 1) used a case–control or prospective study design; 2) evaluated the association between CV intake and CRC risk; 3) presented odds ratio (OR), RR, or hazard ratio (HR) estimates with 95% CI, standard errors (SE), or data necessary to calculate these.	High intake cruciferous vegetable, cabbage, broccoli	Low intake cruciferous vegetable, cabbage, broccoli	CRC Risk 10 Cohort; 23 case-control 1,295,063	Cruciferous **RR=0.82 (0.75; 0.90)** Cabbage **RR=0.76 (0.60; 0.97)** Broccoli	Quality: The range of quality scores was from 4 to 9 on NOS (median=7) **Heterogeneity:** Cruciferous: p<0.01;

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
					subjects 24,275 cases	RR=0.82 (0.65; 1.02)	I^2=66% Cabbage: p=0.23; I^2=58% Broccoli: p=0.05; I^2=55% No publication bias
Woo et al., 2014 Korea [40]	Up to June 20th, 2014	**Inclusions:** (1) original articles with a case-control or Cohort design; (2) articles reporting on cancer risk and diet in the Korean population; (3) studies reporting adjusted OR or RR with 95% CI for the risk of cancer in subjects with the highest category of food intake compared with those with the lowest food intake; and (4) in cases of multiple publications drawn from studies of the same population, only the most recent study was included.	Highest level of vegetable consumption	Lowest level of vegetable consumption	CRC 2 studies	RR=0.51 (0.19; 1.32)	Quality Not performed Heterogeneity p=0.024, I2=80.5% Publication bias Not performed
Zhu et al., 2015 [39]	**Up to December 2014**	**Inclusions:** 1) Cohort; 2) the exposure was legume consumption, including tofu or soybeans, peas, beans, lentils, and other podded plants and all products made of them; 3) the outcome was risk of CRC, incidence of CRC; 4) provided or allowed calculation of RR with 95% CI **Exclusion:** 1) retrospective design; 2) were Non- human, in vitro research, case reports; 3) focused on the recurrence, growth; 4) focused on adenoma; and 5) did not adjust for confounders.	High intake legume	Low intake legume	CRC Risk 14 Cohort 1,903,459 participants 12,261 cases	**RR=0.91 (0.84; 0.98)** CRC men RR=0.92 (0.85; 1.01) CRC Women RR=0.90 (0.78; 1.03)	Quality not reported **Heterogeneity: p=0.01; I^2=40.2%** **Publication bias** Egger p=0.16 Begg p=0.31
Tsé et al., 2014 Australia [37]	**Up to May 2013** ‘	**Inclusion** 1) original data was provided; 2) the association between cruciferous vegetable intake and colorectal neoplasm risk was addressed; 3) the risk point estimate was	High intake total vegetable	Low intake total vegetable	CRC 11 Cohort; 18 case-	OR=0.92 (0.83; 1.01)	Quality not reported **Heterogeneity: p<0.01; I^2=66%**

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
		reported as an OR or RR, or the data was presented such that an OR could be calculated; and 4) the 95% CI was reported, or the data was presented such that the CI could be calculated.			control		**Publication bias** Egger p=0.13
					Colon	**OR=0.84 (0.72; 0.98)**	Quality not reported **Heterogeneity: p<0.01; I^2=64%**
					Rectal	OR=0.99 (0.67; 1.46)	Quality not reported **Heterogeneity: p<0.01; I^2=87%**
Kashino et al., 2015 Japan [38]	**up to December 2014**	**Inclusion:** 1) only studies on Japanese populations living in Japan, 2) presented colorectal cancer risk associated with intakes of total vegetable, green yellow vegetable or green vegetable **Exclusion:** 1) results only for intake of individual vegetable.	Highest vegetable consumption	Lowest consumption	CRC 6 Cohort, 11 case-control	Cohort: RR=1.00 (0.92; 1.10) **case-control: RR=0.75 (0.59; 0.96)**	Quality not reported **Heterogeneity:** Cohort: p=0.52; I^2=0% case-control: p=0.03; I^2=45% **No publication bias**
					Colon 3 Cohort; 5 case-control	Cohort : RR=0.95 (0.83; 1.09) case-control : RR=0.80(0.58; 1.11)	Quality not reported **Heterogeneity:** Cohort: p=0.35; I^2=10% case-control: p=0.18; I^2=36% **No publication bias**
					Rectal 4 Cohort	case-control: RR=1.08 (0.93; 1.26)	Quality not reported **Heterogeneity:** Cohort: p=0.52; I^2=10% case-control: p=0.09; I^2=48% **No publication bias**

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
Vieira et al, 2017 UK [27]	**Up to May 2015**	**Inclusion:** 1) RCT, Cohort or case-control design, 2) report adjusted estimates of the RR and 95% CIs for the association of foods and CRC incidence; 3) for dose–response meta-analysis, studies should provide a quantitative measure of the intake.	Vegetable Dose response Incremental of 100g/day		CRC Risk 11 Cohort or case-control	**RR=0.98 (0.96; 0.99**)	High quality studies but not detailed **Heterogeneity:** p=0.48; I^2=0% **Publication bias:** Egger p=0.92
					Colon 8 Cohort or case-control	**RR=0.97 (0.95; 0.99)**	High quality studies but not detailed **Heterogeneity:** p=0.77; I^2=0% **Publication bias:** Egger p=0.77
					Rectal 8 Cohort or case-control	RR=0.99 (0.96; 1.02)	High quality studies but not detailed **Heterogeneity:** p=0.78; I^2=0% **Publication bias:** Egger p=0.72
			Fruits Dose response Incremental of 100g/day		CRC 13 Cohort or case-control	**RR=0.96 (0.93; 1.00)**	High quality studies but not detailed **Heterogeneity: p<0.001; I^2=68%** **Publication bias:** Egger p=0.07
					Colon 12 Cohort or case-control	RR=0.98 (0.96; 1.01)	High quality studies but not detailed **Heterogeneity:**

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
							P=0.09; I^2=38% **Publication bias:** Egger p=0.55
					Rectal 9 Cohort or case-control	RR=0.98 (0.93; 1.03)	High quality studies but not detailed **Heterogeneity:** **P=0.02; I^2=55%** **Publication bias:** Egger p=0.41
			Legumes Dose response Incremental of 50g/day		CRC 4 Cohort or case-control	RR=1.00 (0.95; 1.06)	High quality studies but not detailed **Heterogeneity:** P=0.20; I^2=33% **None detected**
					Colon 6 Cohort or case-control	RR=0.97 (0.83; 1.15)	**Heterogeneity:** P=0.04; I^2=55%
					Rectal 4 Cohort or case-control	RR=0.99 (0.78; 1.25)	**Heterogeneity:** P=0.14; I^2=45%
SOY							
Tsé et al., 2016, Autralia [41]	Throught May 2014	(1) original data on soy consumption and GI neoplasms risk, that of the esophagus, stomach and/or colorectum, were provided; (2) the risk point estimate was reported as OR or RR, or the data were presented such that an OR could be calculated; (3) the 95 % confidence interval (CI) was reported, or the data were presented such that the CI could be	Soy intake		CRC risk	**OR=0.92 (0.87; 0.97)**	Quality Not reported Heterogeneity p=0.3 Publication bias Egger's p<0.001

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
		calculated.			Colon cancer	**OR=0.92(0.96;0.99)**	Quality Not reported Heterogeneity p=0.163 Publication bias Egger's p<0.001
					Rectal cancer	OR= 0.94 (0.80;1.09)	Quality Not reported Heterogeneity Not reported Publication bias Egger's p<0.001
Zhu et al, 2015 China [39]	Up to December 2014	**Inclusions** 1) a prospective Cohort design; 2) the exposure was legume consumption, including tofu or soybeans, peas, beans, lentils, and other podded plants and all products made of them; 3) the outcome was risk of CRC, incidence of colorectal cancer; 4) provided or allowed calculation of RR with 95% CI **Exclusions:** 1) had a retrospective design; 2) were Non- human, in vitro research, case reports; 3) focused on the recurrence, growth; 4) focused on adenoma; and 5) did not adjust for confounders.	Highest soybeans consumption	Lowest soybeans consumption	CRC risk 3 studies	Soybean **RR = 0.85 (0.73; 0.99)**	Quality Not reported Heterogeneity I^2=40.2%, p=0.01 Publication bias Egger's p=0.16 Begg's p=0.31
Woo et al, 2014 Korea [40]	Up to June 20th, 2014	**Inclusions:** (1) original articles with a case-control or Cohort design; (2) articles reporting on cancer risk and diet in the Korean population; (3) studies reporting adjusted OR or RR with 95% CI for the risk of cancer in subjects with the highest	Highest level of intake	Lowest level of intake	CRC risk	Soybean: OR=1.01 (0.70;1.47)	Quality performed Not reported Heterogeneity I^2=17.6%, p=0.297

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
		category of food intake compared with those with the lowest food intake; and (4) in cases of multiple publications drawn from studies of the same population, only the most recent study was included.					Publication bias: not reported

aRR: adjusted risk ratio, Ca: calcium, case-control: case-control study, CI: confidence interval, Cohort: cohort study, CRA: colorectal adenoma, CRC: colorectal cancer, FU: follow-up, GI: gastro-intestinal, HR: hazard ratio, Mg: magnesium, NS: not specified, NSAID: non-steroidal anti-inflammatory drugs, NOS: Newcastle-Ottawa Scale, OR: odds ratio, RCT: randomised clinical trial, RR: risk ratio, unk: unknown, Vit: vitamin;

A: includes also the comparisons of Vit E + b-Carotene vs placebo; Vit A + b-Carotene vs placebo; Vit E + selenium alone vs placebo; Vit CE + b-Carotene (± simvastatin) vs Placebo (± simvastatin); Vit CE + b-Carotene + selenium + zinc vs placebo. All were had not significant risk ratios

* See calcium section

** not primary outcome

Supplementary Table 2. Components with no protective effect on CRC prevention

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
Vitamine E							
Pais et al., 2013 Romania [46]	Up to May 2009 Cochrane Library, Medline	**Inclusions**: 1) RCT, 2) antioxidants alone or in combination versus placebo or no intervention, 3) reported the incidence of colorectal cancer as primary or secondary outcome 4) global or cancer related mortality 5) participants had to be free of history of cancer (except skin cancer), 6) ≥age 18 years, 2) general populations or from other patients groups primarily with	Vit A, C and E, selenium or b-carotene	placebo or no intervention	CRC incidence 12 RCT N=17,914	Vit E alone: RR =0.99 (0.86; 1.13)	Quality not reported Heterogeneity: Overall: I^2 = 7%, p=0.38 Publication bias: low

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
		non-gastrointestinal diseases. **Exclusions**: 1) antioxidants supplementation through dietary increases in fruits, vegetables or fibers.					
Bjelakovic et al., 2008 Denmark [43]	1945-2007 CENTRAL, MEDLINE, EMBASE, LILACS, SCI-EXPANDED	**Inclusions:** 1) randomised trials, irrespective of blinding, publication status, publication year, or language, 2) adults, 3) antioxidant supplements at any dose, duration, and route of administration 4) compared to placebo or no intervention.	Vit A, C and E, selenium or b-carotene	placebo/no intervention	CRC incidence* 2RCT N=21,114	Vit E alone: RR = 1.10 (0.87; 1.39);	Quality performed with a published scale Heterogeneity: Tau2 = 0.0; Chi2 = 0.57, df = 1 (P = 0.45); I2 =0.0% Test for overall effect: Z = 0.80 (P = 0.42) Publication bias: unk for CRC
Papaioannou et al, 2011 UK[A] [45]	Up to March 2009 Cochrane Library, MEDLINE, PreMED-LINE, CINAHL, EMBASE, Web of Science, BIOSIS and Research Registers UKCRN, MRC Register,	**Inclusions:** 1) RCT, 2) antioxidants (vitamin A, C and E, selenium or b-carotene) with or without other agents, 3) adults, 4) general population 5) compared to no intervention, placebo or agents other than antioxidants, **Exclusions:** none of the inclusions **Population:** healthy populations and in populations with histories of cardiovascular disease; smoking or asbestos exposure; skin cancer; and atrophic gastritis	Vit E alone (studies with event data)	Placebo alone	CRC incidence 2 RCTs N=32,006	RR=1.05 (0.83; 1.33)	Quality performed with a published scale Heterogeneity: Overall: $I^2 = 0\%$, Publication bias: unk for CRC

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
	Current controlled trials						
			Vit E (adjusted for other antioxidants; studies with or without event data)	Placebo alone	CRC incidence 6 RCTs N=not reported	RR=0.99 (0.86;1.14)	Quality performed with a published scale Heterogeneity: Overall: I^2 = 0%, Publication bias: unk for CRC
Liu et al., 2015 China [23]	Up to April 2014 Pubmed	Inclusions: [1] they were cohort studies [2]; the exposure of interest was vitamin or multiple-vitamin supplement intake [3]; the outcome of interest was the incidence of colorectal, colon, or rectal cancer [4]; relative risk (RR) or odds ratio (OR) estimates with 95 % confidence intervals (95 % CI) were reported; Exclusions: Articles with<6 stars were excluded.	highest level vitamin	Lowest level of vitamin	CRC incidence 13 COHORT for Vit E N=unk	Vit E: RR = 0.94 (0.82; 1.32)	Quality performed: NOS Heterogeneity: Vit E: I^2 = 10%; Publication bias: Vit E: p=0.02
Heine-Bröring et al., 2015 [22]	Up to January 2013 Medline, Embase and Cochrane	Inclusions: prospective cohort studies if they reported original and peer-reviewed data on the association of dietary supplement use and colorectal, colon, or rectal cancer incidence. To be included in the meta-analyses, information on ascertainment of colorectal cancer cases, and estimates of the relative risk with 95% confidence intervals (95% CI) were required Exclusions: studies on colorectal adenomas were excluded, Randomized controlled trials and case-control studies	Intake of multivitamins, Vit A, Vit C, Vit E, Vit D, Calcium* and Garlic.	No intake	Colon cancer incidence 5 COHORT for Vit E	Vit E RR = 0.85 (0.72; 1.01)	Quality performed: none Heterogeneity: Vit E I^2=20%; p=0.29 Publication bias: not reported

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
		were excluded					
			Highest level of multivitamins, Vit A, Vit C, Vit E, Vit D, Ca and Garlic.	Lowest level of multivitamins, Vit A, Vit C, Vit E, Vit D, Ca and Garlic.	Colon cancer incidence 5 COHORT for Vit E,	Vit E: **RR = 0.82 (0.67; 0.99)**	Quality performed: none Heterogeneity: Vit E I^2=11%; p=0.34 Publication bias: not reported
Alkhenizan et al. 2007 Saudi Arabia [42]	January 1966-June 2005 Medline, Embase and Cochrane	Inclusions: 1) RCTs, 2) outcomes related to cancer prevention 3) intake of vit E supplements alone or with other supplements 3) >18 years old 4) supplementation was in capsule or tablet form, to be consumed by mouth. Exclusions:	Intake of vitamin E supplement alone or with other supplements	placebo or control	CRC incidence 2 RCTs with vit E alone N= 24,114 (vit E alone)	Vit E Alone: RR=1.05 (0.79; 1.39)	Quality performed: Jadad score Heterogeneity: Not reported for CRC incidence Publication bias: not reported
Arain et al., 2010 UK [44]	January 1999-January 2009 Medline, Embase and Cochrane, OVID data base and other library sources, Google scholar	Inclusions: 1) RCTs Exclusions: 1) combination of vitamins or antioxidant effect 2) outcome of changes at cellular level 3) dichotomous outcome of colorectal cancer	Intake of vit E	placebo or other supplement	CRC incidence 4 RCTs (2 studies 300UI/day, one 400UI/day, one 50mg/day)	Vit E RR= 0.89 (0.76; 1.05)	Quality performed: CONSORT scoring Heterogeneity: I^2=7%; p=0.36 Publication bias: not reported
Vitamin C							
Heine-	Up to January	Inclusions: prospective cohort studies if	Intake of	No intake	Colon	Vit C	Quality

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
Bröring et al., 2015 [22]	2013 Medline, Embase and Cochrane	they reported original and peer-reviewed data on the association of dietary supplement use and colorectal, colon, or rectal cancer incidence. To be included in the meta-analyses, information on ascertainment of colorectal cancer cases, and estimates of the relative risk with 95% confidence intervals (95% CI) were required Exclusions: studies on colorectal adenomas were excluded, Randomized controlled trials and case-control studies were excluded	multivitamins, Vit A, Vit C, Vit E, Vit D, Calcium* and Garlic.		cancer incidence 3 COHORT for Vit C	RR = 0.87 (0.63; 1.21),	performed: none Heterogeneity: Vit C I^2=77%; p=0.01 Publication bias: not reported
			Highest level of multivitamins, Vit A, Vit C, Vit E, Vit D, Ca and Garlic.	Lowest level of multivitamins, Vit A, **Vit C,** Vit E, Vit D, Ca and Garlic.	**Colon cancer incidence** 3 COHORT for Vit C,	Vit C: RR = 0.85 (0.68; 1.05)	Quality performed: none Heterogeneity: Vit C I^2=11%; p=0.33 Publication bias: not reported
Papaioannou et al, 2011 UK[A] [45]	Up to March 2009 Cochrane Library, MEDLINE, PreMED-LINE, CINAHL, EMBASE, Web of Science, BIOSIS and Research	**Inclusions:** 1) RCT, 2) antioxidants (vitamin A, C and E, selenium or b-carotene) with or without other agents, 3) adults, 4) general population 5) compared to no intervention, placebo or agents other than antioxidants, **Exclusions:** none of the inclusions **Population:** healthy populations and in populations with histories of cardiovascular disease; smoking or asbestos exposure; skin cancer; and	Vit C (adjusted for other antioxidants; studies with no event data)	No Vit C (adjusted for other antioxidants)	**CRC incidence** 2 RCTs N=not reported	RR= 0.84 (0.64;1.10)	Quality performed with a published scale Heterogeneity: Overall: I^2 = 0%, Publication bias: unk for CRC

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
	Registers UKCRN, MRC Register, Current controlled trials	atrophic gastritis					
Antioxidants combination or vitamins combination with other components							
Heine-Bröring et al., 2015 [22]	Up to January 2013 Medline, Embase and Cochrane	**Inclusions:** prospective Cohort studies if they reported original and peer-reviewed data on the association of dietary supplement use and colorectal, colon, or rectal cancer incidence. To be included in the meta-analyses, information on ascertainment of CRC cases, and estimates of the RR with 95% CI were required **Exclusions:** studies on colorectal adenomas, RCTs and case-control	Intake of multivitamins	No intake	**CRC incidence** 16 Cohort for multivitamins	Multivitamins: **RR=0.92(0.86;0.98)**	Quality performed: none Heterogeneity: Multivitamins: I^2=0%; p=0.43 Publication bias: not reported
Pais et al., 2013 Romania [46]	Up to May 2009 Cochrane Library, Medline	**Inclusions**: 1) RCT, 2) antioxidants alone or in combination versus placebo or no intervention, 3) reported the incidence of CRC as primary or secondary outcome 4) global or cancer related mortality 5) participants had to be free of history of cancer (except skin cancer), 6) ≥age 18 years, 2) general populations or from other patients groups primarily with non-GI diseases. **Exclusions**: 1) antioxidants supplementation through dietary increases in fruits, vegetables or fibers.	Vit A, C and E, selenium or β-carotene	placebo or no intervention	CRC incidence 4 RCT N=52,262	Overall antioxidant combination: RR=0.98 (0.89;1.07) Vit C combination RR=0.83(0.69;1.00) Vit E combination RR=0.97(0.85;1.10)	Quality not reported Heterogeneity: Overall: I^2 = 7%, p=0.38 Publication bias: low
Bjelakovic et al., 2008 Denmark	1945-2007 Central,	**Inclusions:** 1) RCT, irrespective of blinding, publication status, publication year, or language, 2) adults, 3)	antioxidant supplements (Vit A, C and	placebo/no intervention	CRC incidence*	Overall: RR=0.97(0.86; 1.09)	Quality performed with a published scale

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
[43]	Medline, Embase, Lilacs, Sci-Expanded	antioxidant supplements at any dose, duration, and route of administration 4) compared to placebo or no intervention.	E, selenium or β-carotene)		20 RCT N=211,818 for all GI cancer outcomes (unk for CRC)		Heterogeneity: I^2 = 20%, Publication bias: unk for CRC
Papaioannou et al, 2011 UK[A] [45]	Up to March 2009 Cochrane Library, MEDLINE, PreMED-LINE, CINAHL, EMBASE, Web of Science, BIOSIS and Research Registers UKCRN, MRC Register, Current controlled trials	**Inclusions:** 1) RCT, 2) antioxidants (vitamin A, C and E, selenium or β-carotene) with or without other agents, 3) adults, 4) general population 5) compared to no intervention, placebo or agents other than antioxidants, **Exclusions:** none of the inclusions **Population:** healthy populations and in populations with histories of CVD; smoking or asbestos exposure; skin cancer; and atrophic gastritis	Antioxidants (Vit A, C and E, selenium or β-carotene) +/- aspirin, simvastatin, ramipril	No antioxidants +/-aspirin, simvastatine, ramipril	CRC incidence 9 RCT n=148,922	RR=1.00(0.88; 1.13) Random effect model	Quality performed with a published scale Heterogeneity: I^2 = 25%, p=0.22 Publication bias: none
Alkhenizan et al. 2007 Saudi Arabia [42]	January 1966-June 2005 Medline, Embase and Cochrane	**Inclusions:** 1) RCTs, 2) outcomes related to cancer prevention 3) intake of Vit E supplements alone or with other supplements 3) >18 years old 4) supplementation was in capsule or tablet form, to be consumed by mouth.	Intake of vitamin E supplement alone or with other supplements	placebo or control	**CRC incidence** 4 RCTs (2 RCTs with vit E alone) N= 91,099 (all studies) 24,114 (vit E alone)	Vit E with other supplements: RR=0.95(0.81;1.12) Fixed effect model	Quality performed: Jadad score: high Heterogeneity: Not reported for CRC incidence Publication bias: not reported

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
β Carotene							
Druesne-Pecollo et al., 2010 France [47]	up to April 2009 Pubmed	**Inclusions:** 1) RCTs, 2) original article 3) intervention consisting in β-carotene supplementation (given alone or in combination with other antioxidants), 4) primary cancer as outcome, 5) reporting the RR and 95% CIs of cancers at the end of the intervention (excepted for the Women's Health Study, which provided data 2 years after the end of the intervention)	β-carotene alone 20mg, 30mg and 50mg daily, FU: 2 to 17 yrs	Placebo	CRC incidence 3 RCTs N=91,080	β-carotene alone: RR=0.99(0.83; 1.18)	Quality performed: not done Heterogeneity: I^2=94% Publication bias: not reported
			β-carotene (alone and in combination)	Placebo	**CRC incidence** 4 RCTs for overall 3 RCTs for alone 5 RCTs for combination N=151,118 for overall, 91,080 for alone, 89,171 for combination,	Overall: RR=0.96(0.85-1.09) β-carotene in combination: RR=0.94(0.79; 1.11) Subgroup: 20-30mg/day : RR=0.96(0.84;1.09), Majority of Men RR=0.99(0.93; 1.05) Majority of Women RR=0.99(0.93; 1.06)	Quality performed: not done Heterogeneity: Overall: I^2=93% Alone: I^2=94% Combined: I^2=70% Publication bias: not reported

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
Pais et al., 2013 Romania[B] [46]	Up to May 2009 Cochrane Library, Medline	**Inclusions**: 1) RCT, 2) antioxidants alone or in combination versus placebo or no intervention, 3) reported the incidence of CRC as primary or secondary outcome 4) global or cancer related mortality 5) participants had to be free of history of cancer (except skin cancer), 6) ≥age 18 years, 2) general populations or from other patients groups primarily with non-GI diseases. **Exclusions**: 1) antioxidants supplementation through dietary increases in fruits, vegetables or fibers.	β-carotene alone Dose 6–50 mg/day	placebo or no intervention	CRC incidence 4 RCTs N=16,913	β-carotene alone: RR=1.09(0.92; 1.29)	Quality not reported Heterogeneity: Unk for β-carotene Publication bias: Unk for β-carotene
			β-carotene (alone and in combination)	placebo or no intervention	CRC incidence 4 RCTs N=16,913	β-carotene combination: RR=0.99(0.89; 1.11)	Quality not reported Heterogeneity: Unk for beta carotene Publication bias: Unk for beta carotene
Bjelakovic et al., 2008 Denmark [43]	1945-2007 Central, Medline, Embase, LILACS, sci-expanded	**Inclusions:** 1) RCT, irrespective of blinding, publication status, publication year, or language, 2) adults, 3) antioxidant supplements at any dose, duration, and route of administration 4) compared to placebo or no intervention.	β-carotene alone	placebo/no intervention	CRC incidence* 3 RCT n=36,782	β-carotene alone: RR=1.09(0.79;1.51);	Quality performed with a published scale Heterogeneity: (P = 0.12); I^2 =53% Test for overall effect: Z = 0.51 (P = 0.61) Publication bias:

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
							unk for CRC
			β-carotene (alone and in combination)	placebo/no intervention	CRC incidence* 20 RCT N=211,818 for all GI cancer outcomes (unk for CRC) One MA for each group	β-carotene and Vit A: RR=0.97(0.76;1.25); β-carotene and Vit E RR=1.20(0.89;1.63); β-carotene, vit C, and vit E: RR=0.84(0.65;1.07); β-carotene, Vit C, Vit E, and selenium RR=0.88(0.49; 1.58)	Quality performed with a published scale Heterogeneity non-applicable. β-carotene and vit A: Test for overall effect: Z = 0.20 (P = 0.84) β-carotene and Vit E Test for overall effect: Z = 1.18 (P = 0.24) β-carotene, vit C, and vit E: Test for overall effect: Z = 1.44 (P = 0.15) β-carotene, vit C, vit E, and selenium Test for overall effect: Z = 0.42 (P = 0.67) Publication bias: unk for CRC
Asano et al., 2004 Canada [48]	up to September 2003 Medline, preMedline,	**Inclusion:** RCTs that compared a NSAID intervention to a placebo or an alternate intervention for the prevention of CRAs or CRC were included, provided the trials reported at least one of the following	Aspirin 325 mg and/or β-carotene 50 mg every other day	placebo	CRC incidence 1 RCT¶	RR=1.15 (0.80; 1.64)	Not specified

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
	Embase and Central	outcomes: the number of patients who developed 1) at least one CRA, 2) more than one CRA, 3) at least one CRA that was 1 cm or greater, 4) at least one pathologic diagnosis of a tubulo-villous or villous CRA, 5) the new diagnosis of CRC, or 6) a change in polyp burden ("polyp burden" defined for each trial) **Exclusions:** not specified					
Papaioannou et al, 2011 UK [45]	Up to March 2009 Cochrane Library, MEDLINE, PreMED-LINE, CINAHL, EMBASE, Web of Science, BIOSIS and Research Registers UKCRN, MRC Register, Current controlled trials	**Inclusions:** 1) RCT, 2) antioxidants (vitamin A, C and E, selenium or β-carotene) with or without other agents, 3) adults , 4) general population 5) compared to no intervention, placebo or agents other than antioxidants, **Exclusions:** none of the inclusions **Population:** healthy populations and in populations with histories of cardiovascular disease; smoking or asbestos exposure; skin cancer; and atrophic gastritis	β-carotene (± aspirin; studies with or without event data) FU: 6 to 12 yrs	No β-carotene (± aspirin)	**CRC incidence** 3 RCT N=36,812	β-carotene (± aspirin) RR=1.09(0.78;1.51),	Quality performed: yes, with authors scale Heterogeneity: I^2=54% Publication bias: not reported
			β-carotene (± aspirin; and adjusted for other antioxidants; studies with or without event data) Follow up 6 to 12 Years	No β-carotene (± aspirin; and adjusted for other antioxidants))	**CRC incidence** 4 RCT N=not reported	βcarotene (± aspirin) RR=1.11 (0.84;1.47)	Quality performed: yes, with authors scale Heterogeneity: I^2=26% Publication bias: not reported
SELENIUM							
Papaioannou et al., 2011	Up to March 2009	**Inclusions:** 1) RCT, 2) antioxidants (vitamin A, C and E, selenium or b-	Selenium alone	Placebo alone	**CRC incidence**	Selenium 200ug/d RR=0.77(0.37; 1.62)	Quality performed: yes,

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
UK [45]	Cochrane Library, MEDLINE, PreMED-LINE, CINAHL, EMBASE, Web of Science, BIOSIS and Research Registers UKCRN, MRC Register, Current controlled trials	carotene) with or without other agents, 3) adults , 4) general population 5) compared to no intervention, placebo or agents other than antioxidants, **Exclusions:** none of the inclusions **Population:** healthy populations and in populations with histories of cardiovascular disease; smoking or asbestos exposure; skin cancer; and atrophic gastritis	Follow up 5.5 to 8 Years		2 RCT N=18,698		with authors scale Heterogeneity: I^2=68% Publication bias: not reported
Pais et al., 2013 Romania [46]	Up to May 2009 Cochrane Library, Medline	**Inclusions**: 1) RCT, 2) antioxidants alone or in combination versus placebo or no intervention, 3) reported the incidence of colorectal cancer as primary or secondary outcome 4) global or cancer related mortality 5) participants had to be free of history of cancer (except skin cancer), 6) ≥age 18 years, 2) general populations or from other patients groups primarily with non-GI diseases. **Exclusions**: 1) antioxidants supplementation through dietary increases in fruits, vegetables or fibers.	Vit A, C and E, selenium or b-carotene	placebo or no intervention	CRC incidence 3 RCT (alone) 4 RCT (combinatio n)	Selenium alone (100-200ug/day) RR=0.77(0.36; 1.62) Selenium combination RR=0.88(0.55;1.40)	Quality not reported Heterogeneity: Overall: I^2 = 7%, p=0.38 Publication bias: low
Bjelakovic et al., 2008 Denmark [43]	1945-2007 CENTRAL, MEDLINE, EMBASE, LILACS, SCI-	**Inclusions:** 1) randomised trials, irrespective of blinding, publication status, publication year, or language, 2) adults, 3) antioxidant supplements at any dose, duration, and route of administration 4) compared to placebo or	Vit A, C and E, selenium or β-carotene	placebo/no intervention	CRC incidence* 1RCT N=1,312	Selenium alone: RR=0.48(0.22;1.05);	Quality performed with a published scale Heterogeneity: not applicable

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
	EXPANDED	no intervention.					Test for overall effect: Z = 1.84 (P = 0.066) Publication bias: unk for CRC
TEA							
Sun et al., 2006 **USA** [52]	Jan 1966 to Jul 2005	**Inclusion:** 1) the number of CRC cases and Cohort studied; and/or 2) the OR or RR and its corresponding 95% CI, for highest versus non/lowest level of tea intake	Green tea Highest tea consumption (varying cut-off 5 to 10 cup/day; 3500-8000g; daily; ever)	Green tea Lowest tea consumption or non drinkers (varying cut-off: 0-3 cups/days; rarely; <daily; rarely; never)	CRC risk 4Co; 4CC	**Overall** **OR=0.82(0.69; 0.98)** Cohort OR=0.97(0.82; 1.16) **case-control** **OR=0.74(0.63; 0.86)** <u>Subgroup (overall)</u> Colon cancer OR=0.86(0.73; 1.00) Rectal cancer OR=0.99(0.7; 1.37) Women: OR=0.52(0.25; 1.05) Men: OR=0.89(0.73; 1.08)	Quality not reported **Heterogeneity:** Overall: p=0.03 case-control: p=0.18 Cohort p=0.18 **Publication bias:** Egger=0.98
			Black tea Highest tea consumption (varying cut-off 1 to 5 cup/day; >160 g/month; daily; drinker)	Black tea Lowest tea consumption (varying cut-off <1 to 3 cup/day; >800 g/month; rarely; non-drinker)	CRC risk 7Co; 13 case-control	**Overall** OR=0.99(0.87; 1.13) Cohort OR=1.02(0.76; 1.34) case-control OR=0.92(0.78; 1.09) <u>Subgroup (overall)</u> Colon cancer OR=1.02(0.88; 1.18) Rectal cancer	Quality not reported **Heterogeneity:** Overall: p<0.01 case-control: p<0.01 Cohort p=0<0.01 **Publication bias:**

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
						OR=0.91(0.73; 1.12) **Women:** **OR=0.82(0.70; 0.95)** Men: OR=1.15(0.89; 1.50)	Egger=0.1
Wang et al., 2012 **China** [49]	up to May, 2012	**Inclusions**: 1) case-control study; 2) tested the association between green tea and CRC risk; 3) the cancer type did not contain adenocarcinoma; 4) the diagnoses of CRC was confirmed either histological, pathologically or cytological; 5) the site of cancer included colon, rectum, or colorectum; 6) the adjusted OR and relevant corresponding 95% CIs were reported, for highest vs. non/lowest level of green tea intake.	Highest green tea intake (varying cut-off 1 to 7 cup/day; >8500 g/month; drinker)	Lowest green tea intake (varying cut-off <1 cup/day; <g/month; non drinkers)	CRC 13 case-control 12,636 cases and 38,419 controls	**Overall** OR=0.99(0.87; 1.13)	**Heterogeneity:** P=0.49; No publication bias
					Colon cancer risk 8CC	OR=0.96(0.08; 1.16)	**Heterogeneity:** P<0.01; I^2=0.61;
					Rectal cancer risk 6CC	OR=0.96(0.73; 1.26)	**Heterogeneity:** P<0.01; I^2=0.68;
Zhang et al., 2015 **China** **[50]**	**up to October 2013**	**Inclusions:** 1) prospective observational design; 2) address the association between tea consumption and the risk of cancer incidence; and 3) includes comparisons between high and low tea consumption (with >2 categories) and estimates of the effect as RR, HR or OR with 95% CIs	Highest tea consumption (green, black and mixed tea)- no assessment of cut-off	Lowest tea consumption (green, black and mixed tea)- no assessment of cut-off	Colon cancer risk 11 Cohort 3871 cases; 1 154 458 patients FU:4.3- 19.0 years	RR=0.95(0.84; 1.07) Dose–response analysis for one cup day increment RR=0.98(0.93; 1.02) **Subgroup:** Women: RR=0.98(0.93; 1.03) Men: RR=0.91(0.78; 1.06)	**Heterogeneity:** P=0.08; I^2=34.5% No publication bias
					Rectal cancer risk 11 Cohort	RR=1.03(0.88; 1.21) Dose–response analysis for one	**Heterogeneity:** P=0.16; I^2=27.2%

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
					9716 cases; 1 154 458 patients FU:4.3- 20.0 years	cup/day increment: RR=1.01(0.97; 1.05) <u>Subgroup:</u> Women: RR=0.98(0.92; 1.05) Men: RR=1.07(0.98; 1.17)	No publication bias
Vieira et al., 2017 UK [27]	**Up to May 2015**	**Inclusion:** 1) RCT, Cohort or case-control design, 2) report adjusted estimates of the RR and 95% CIs for the association of foods and CRC incidence; 3) for dose–response meta-analysis, studies should provide a quantitative measure of the intake.	Dose response Incremental of 1 cup/day		CRC risk 8 case-control 16251 Cases	OR=0.99(0.97; 1.01)	**No assessment of quality** **Heterogeneity:** P=0.05; I^2=44% **Publication bias:** Egger p=0.42
					Colon cancer risk 6CC 13244 cases	OR=0.99(0.94; 1.03)	**Heterogeneity:** P<0.01; I^2=75% **Publication bias:** Egger p=0.33
					Rectal cancer risk 9CC 4621 cases	OR=0.99(0.97; 1.02)	**Heterogeneity:** P=0.47; I^2=0% **Publication bias:** Egger p=0.04
Chen et al., 2017 China [51]	**Up to June 2016**	**Inclusions**: 1) case-control or Cohort study; b) evaluated the associations between tea consumption and CRC risk; 3) all CRC cases were either histopathologically or cytologically confirmed; 4) provided the quantity of CRC cases and controls or person-years;	Highest tea consumption (green, black and mixed tea)- no assessment of cut-off	Lowest tea consumption (green, black and mixed tea)- no assessment of cut-off	CRC incidence 17Co 12CC 1,642,007 patients	OR=0.93(0.87; 1.00) Dose response analysis: consumption of 1c/d OR=1.01(0.99; 1.03)	Assessment of individual quality study **Heterogeneity:** P<0.01; I^2=43%

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
		5) RRs or ORs with corresponding 95% CIs, especially for highest vs. non/lowest level of tea consumption				Subgroup: Women: **OR=0.86(0.78; 0.94)** Men: RR=0.98(0.85; 1.12)	**Publication bias:** Egger p=0.04
					Colon cancer risk 22Co or case-control	OR=0.92 (0.79 1.06)	**Heterogeneity:** P<0.01; I^2=42%
					Rectal cancer risk 19 Cohort or case-control	**OR=0.91(0.85; 0.99)**	**Heterogeneity:** P<0.05; I^2=31%
ALLIUM AND GARLIC							
Zhu et al., 2014 [54]	up to October 2013	**Inclusions** (1) Cohort or case-control; (2) relationship of allium vegetables or garlic supplements and CRC risk; and (3) the study provided or allowed the calculation of RR with 95% CIs	High intake allium vegetable	Low intake allium vegetable	CRC Risk 20 case-control or Cohort	RR=1.06(0.96; 1.17) Dose response once-per-week increment RR=1.01(1.00; 1.02)	Quality not reported **Heterogeneity:** p=0.94; I^2=0% Publication bias Egger p=0.35
Turati et al., 2014 Italy [55]	April 2014	**Inclusions** 1) had a case-control or Cohort study design, 2) the outcome was colorectal (or colon, or rectal) cancer or colorectal adenomatous polyps incidence/death, 3) examined the association with allium vegetables (including garlic, onions, leeks, and others), 4) provided the RR estimates with their CIs, or data necessary to calculate them **Exclusion:** No studies were excluded a priori for weakness of design or data			CRC risk 16 Studies	Garlic overall RR=0.85 (0.72;1.00) Garlic case-control studies **RR=0.76 (0.67;0.85)** Garlic Cohort studies RR=0.99 (0.80;1.23) Onion RR=0.85 (0.70;1.04) Onion case-control **RR=0.74 (0.56;0.98)**	Quality not reported **Heterogeneity:** p = 0.017, I^2 = 57.2% Publication bias Egger p=0.35

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
		quality				Onion Cohort RR=1.04 (0.86;1.26) Total allium overall RR=0.78 (0.56;1.06) case-control RR=0.69 (0.43;1.09) Cohort RR=0.99 (0.77;1.27)	
					Colon cancer risk	Garlic RR=0.90 (0.75;1.08) Onion RR=0.72(0.44;1.19)	
					Rectal cancer risk	Garlic **0.76 (0.59; 0.98)** Onion 0.70 (0.39; 1.25)	
Heine-Bröring et al., 2015 [22]	Up to January 2013 Medline, Embase and Cochrane	**Inclusions:** prospective Cohort studies if they reported original and peer-reviewed data on the association of dietary supplement use and colorectal, colon, or rectal cancer incidence. To be included in the meta-analyses, information on ascertainment of CRC cases, and estimates of the RR with 95% CI were required **Exclusions:** studies on colorectal adenomas, RCTs and case-control	Intake of multivitamins, Vit A, Vit C, Vit E, Vit D, Calcium* and Garlic.	No intake	CRC incidence 2 Cohort for Garlic	Garlic RR=1.24(0.99; 1.54)	Quality performed: none Heterogeneity: Garlic I^2=0%; p=0.34 Publication bias: not reported
Hu et al., 2014 China [53]	**up to October 2013**	Inclusions: (1) Cohort; (2) evaluated the association between garlic consumption and risk of colorectal cancer; and (3) reported HR or RR with corresponding 95%CI, or data necessary to calculate them	Overall garlic intake		CRC Risk 5 Cohort 335,923 subjects	RR=1.03(0.83; 1.28)	High quality studies (8 or 9 on the NOS) **Heterogeneity:** p=0.54; I^2=0%

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
					4,610 cases follow up 3.3 years to 24 years		
			Garlic Raw and cooked		CRC Risk 4 Cohort	RR=1.07(0.95;1.19), Subgroup : Males RR=1.18(0.99; 1.41) Females RR=1.04(0.80; 1.30)	High quality studies **Heterogeneity:** p=0.66; I^2=0% publication bias: Egger p=0.50
					Colon cancer Risk 4 Cohort	RR=1.07(0.94; 1.21)	High quality studies **Heterogeneity:** p=0.63; I^2=0% publication bias: Egger p=0.23
					Rectal cancer 3 Cohort	RR=1.02(0.90; 1.17)	High quality studies **Heterogeneity:** p=0.93; I^2=0% publication bias: Egger p=0.59
			Garlic supplement		CRC Risk 5 Cohort	RR=1.12(0.96; 1.31)	High quality studies **Heterogeneity:** p=0.47; I^2=11% publication bias:

Study Country (Reference)	**Search period and databases searched**	**Inclusion / exclusion criteria**	**Intervention**	**Control**	**Outcomes**	**Results**	**Quality score Heterogeneity Publication bias**
							Egger p=0.61
					Colon cancer Risk 3 Cohort	RR=1.01(0.77; 1.32)	High quality studies **Heterogeneity:** p=0.47; I^2=15% publication bias: Egger p=0.58
					Rectal cancer 3 Cohort	RR=1.17(0.74; 1.83)	High quality studies **Heterogeneity:** p=0.41; I^2=0% publication bias: Egger p=0.31
Vitamin D							
Liu et al., 2015 China [23]	Up to April 2014 Pubmed	Inclusions: [1] they were cohort studies [2]; the exposure of interest was vitamin or multiple-vitamin supplement intake [3]; the outcome of interest was the incidence of colorectal, colon, or rectal cancer [4]; relative risk (RR) or odds ratio (OR) estimates with 95 % confidence intervals (95 % CI) were reported; [5] Newcastle-Ottawa Scale (NOS) quality grade for cohort studies in meta-analyses [69] was >6.	highest level vitamin	Lowest level of vitamin	CRC incidence 17 CO for Vit D N=unk	Vit D: **RR = 0.87 (0.77; 0.99)**	Quality performed: NOS, only >6 Heterogeneity: Vit D: I^2 = 41%; Publication bias: Vit D: p=0.51

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
		Exclusions: Articles with<6 stars were excluded.					
Heine-Bröring et al., 2015 [22]	Up to January 2013 Medline, Embase and Cochrane	Inclusions: prospective cohort studies if they reported original and peer-reviewed data on the association of dietary supplement use and colorectal, colon, or rectal cancer incidence. To be included in the meta-analyses, information on ascertainment of colorectal cancer cases, and estimates of the relative risk with 95% confidence intervals (95% CI) were required Exclusions: studies on colorectal adenomas were excluded, randomized controlled trials and case-control studies were excluded	Intake of multivitamins, Vit A, Vit C, Vit E, Vit D, Calcium* and Garlic.	No intake	CRC incidence 5 Cohort for Vit D	Vit D RR = 0.92 (0.78; 1.09)	Quality performed: none Heterogeneity: Vit D I^2=54%; p=0.07 Publication bias: not reported
			Highest level of multivitamins, Vit A, Vit C, Vit E, Vit D, Ca and Garlic.	Lowest level of multivitamins, Vit A, Vit C, Vit E, Vit D, Ca and Garlic.	CRC incidence 4 COHORT for Vit D	Vit D RR = 0.87 (0.62-1.22)	Quality performed: none Heterogeneity: Vit D: I^2=67%; p=0.03 Publication bias: not reported
Chung et al., 2011 USA [56]	Up to July 2011 MEDLINE and Central	**Inclusions:** articles about human participants published in English-language journals. RCT **Exclusions:** studies that enrolled pregnant women only or measured vitamin D status only during pregnancy and RCTs comparing different dosages of vitamin D supplementation without a control group that did not receive vitamin D supplementation. We excluded short-term (1 month) RCTs and trials that used synthetic vitamin D analogues (for example, oxacalcitriol or paricalcitol)	Vit D 100,000UI/4 months for 5 years Follow-up: 5 years	Placebo	CRC incidence 1 RCT N= 2686 Vit D	HR=1.02 (0.60-1.74)	Quality performed yes: fair Heterogeneity: unk Publication bias: unk

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
		Population: Elderly 65-85 for vit D alone, and post-menopausal women > 40 years old un Vit D+Ca					
Ma et al., 2011 China [57]	Up to October 2010 MEDLINE and EMBASE	Studies were included in the meta-analysis if they met the following criteria: prospective design; the study of interest was the intake of vitaminD or the levels of 25(OH)D in the blood (plasma or serum); the outcome of interest was colorectal, colon, or rectal cancer; and the relative risk (RR) estimates with 95%CIs (or data to calculate these) were reported. Where data sets overlapped or were duplicated, only the most recent information was included. All	Highest category of vit D intake FU : 4-13years.	Lowest category of vit D intake	CRC incidence 8 COHORT and 1 case-control N=6,466	**RR = 0.88 (0.80; 0.96)**	Quality performed NOS, 6 or 7 stars Heterogeneity: I^2 = 27%, p=0.19 Publication bias: unk
Vitamin D and Calcium							
Carroll et al., 2010 UK [58]	up to January 2010 Cochrane Library, MEDLINE, PreMEDLINE, CINAHL, EMBASE, Web of Science, Biological Abstracts, the National Research Register, and Current	**Inclusions:** 1) RCTs of calcium (with or without other chemopreventive agents) 2) adults with FAP, HNPCC, or a history of colorectal adenomas, or with no increased baseline risk of CRC 3) comparators were specified as either placebo or agents other than calcium, 4) outcomes included the recurrence of adenomas or advanced adenomas, or the occurrence of colorectal cancer. **Population:** Populations with no history of adenomas or CRC.	Calcium 1000-1500mg/day + Vit D 400-1100 UI/d Follow up: 4 or 7 years	Calcium with or without other chemopreventive agents versus placebo (with or without other interventions)	CRC incidence 2 RCTs N=37,016	1) Ca + Vit D: RR=1.08(0.87; 1.34) 2) Ca+/- Vit D: RR=0.62(0.11; 3.40)	Quality not reported Heterogeneity: Ca + Vit D: I^2=0%. Ca+/- Vit D: I^2=58% Publication bias: Not reported

Study Country (Reference)	Search period and databases searched	Inclusion / exclusion criteria	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
	Controlled Trials						
Chung et al., 2011** USA [56]	Up to July 2011 MEDLINE and Central	**Inclusions:** articles about human participants published in English-language journals. RCT **Exclusions:** studies that enrolled pregnant women only or measured Vit D status only during pregnancy and RCTs comparing different dosages of Vit D supplementation without a control group that did not receive Vit D supplementation. We excluded short-term (1 month) RCTs and trials that used synthetic Vit D analogues (for example, oxacalcitriol or paricalcitol) **Population:** Elderly 65-85 for vit D alone, and post-menopausal women > 40 years old un Vit D+Ca	Vit D + calcium Follow-up: 7 years	Placebo	CRC incidence 1 RCT N=36,282	HR=1.08(0.86; 1.34)	Quality performed yes: good Heterogeneity: unk Publication bias: unk

aRR: adjusted risk ratio, Ca: calcium, CI: confidence interval, CRA: colorectal adenoma, CRC: colorectal cancer, FU: follow-up, GI: gastro-intestinal, HR: hazard ratio, Mg: magnesium, NS: not specified, NSAID: non-steroidal anti-inflammatory drugs, NOS: Newcastle-Ottawa Scale, OR: odds ratio, RCT: randomised clinical trial, RR: risk ratio, unk: unknown, Vit: vitamin;

A: includes also the comparisons of Vit E + b-Carotene vs placebo; Vit A + b-Carotene vs placebo; Vit E + selenium alone vs placebo; Vit CE + b-Carotene (± simvastatin) vs Placebo (± simvastatin); Vit CE + b-Carotene + selenium + zinc vs placebo. All were had not significant risk ratios

* See calcium section; ** not primary outcome

Supplementary Table 3. Component with unclear effect on CRC prevention

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
COFFEE AND CAFFEINE							
Giovannuci et al., 1998 **USA** [59]	**Up to 1997** **Medline and cancerlit**	**Inclusion:** all pertinent publications on coffee consumption and risk of CRC.	Highest coffee consumption (approx. 4 cups per day) FU: 1-8yrs	Lowest coffee consumption (approx. 1 cup per day)	CRC risk 12 case-control; 5 Cohort 6192 Cases	**case-control and Cohort RR=0.76(0.66; 0.89)** **case-control: RR=0.72(0.61; 0.84)** Cohort: RR=0.97(0.73; 1.29)	Quality not reported **Heterogeneity:** case-control and Cohort, p<0.01 case-control: p<0.01 Cohort; p=0.83
Je et al., 2009 **USA** [60]	**Up to June 2008** **Medline**	**Inclusion:** prospective Cohort studies on the association between coffee consumption and CRC incidence.	Highest coffee consumption (varying cut-off from 1 to 6)	Lowest coffee consumption (varying cut-off)	CRC risk 12Co 646,848 patients and 5,403 cases Fu of 9.8 years	**Cohort:** RR=0.91(0.81; 1.02)	Quality not reported **Heterogeneity:** Cohort: p=0.73; I^2=0% **Publication bias:** Begg's and Egger's tests > 0.4

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
Galeone et al., 2010 Italy [61]	**1966 to May 2010** **Medline**	**Inclusions:** 1) quantitative estimate; (2) at least one of the following: the 95% CI, or standard error, or the distribution of cases and controls in coffee consumption categories, or the p-value for the difference of the OR from unity **Exclusions:** data for caffeine rather than coffee, or if they were based on data updated later, or if part of pooled analyses	Drinkers FU: 1-8yrs	Non/occasional drinkers	CRC incidence 13 studies; 9568 cases	**OR=0.83(0.73;0.95)**	Quality: not reported **Heterogeneity:** p<0.01; I^2=80% **Publication bias:** None overall
					Colon cancer incidence 11 studies; 7537 cases	OR=0.93(0.81; 1.07)	Quality: not reported **Heterogeneity:** p<0.01; I^2=82%
					Rectal cancer incidence 10 studies, 4594 cases	OR=0.98(0.85; 1.13)	Quality: not reported **Heterogeneity:** p<0.01; I^2=71%
			Increment of 1 cup/day		CRC incidence 13 studies; 9380 cases	**OR=0.94(0.91;0.98)**	Quality: not reported **Heterogeneity:** p<0.01; I^2=69%
					Colon cancer incidence 12 studies; 7713 cases	**OR=0.95(0.92;0.98)**	Quality: not reported **Heterogeneity:** p<0.01; I^2=61%
					Colon cancer incidence	**OR=0.97(0.95;0.99)**	Quality: not reported **Heterogeneity:** P=0.34; I^2=10%

Study Country (Reference)	**Search period and databases searched**	**Inclusions / exclusions**	**Intervention**	**Control**	**Outcomes**	**Results***	**Quality score Heterogeneity Publication bias**
Li et al., 2013 China [62]	**May 2011** **MEDLINE, the Cochrane Controlled Trials Register, EMBASE, Science Citation Index and PubMed**	**Inclusions:** 1) a quantitative estimate of the relationship; and 2) at least one of the 95%CI or the standard error or the distribution of cases and controls in coffee consumption categories.	Highest coffee consumption (varying cut-off)	Lowest/non coffee consumption (varying cut-off)	CRC risk 25 case-control, 16Co case-control : 15 522 cases, Cohort 953 669 participants and 10 443 cases FU: 10.5 years	**Cohort** OR=0.91(0.81;1.02) **Subgroup :** Colon cancer **OR=0.79(0.67;0.95)** Rectal cancer: OR=0.95(0.79; 1.15) Colorectal women : OR=0.93(0.81; 1.05) Colorectal men OR=0.97(0.87; 1.08)	Quality not reported **Heterogeneity:** Cohort: p<0.01; I^2=64% **Publication bias:** Begg p=0.63 Egger=0.69
Akter et al., 2016 Japan [63]	**Up to August 2015** **Medline and Ichushi**	**Inclusions:** Only studies on Japanese populations living in Japan were included, written in English or Japanese	Highest coffee consumption (varying cut-off)	Lowest coffee consumption (varying cut-off)	CRC risk 9 case-control and 4 Cohort (1 Cohort included death and was removed in this sensitivity analysis)	RR=0.98 (0.80;1.22)	Quality score; not done for subgroup Heterogeneity: not done for subgroup Publication bias: not done for subgroup
Gan et al., 2017 China [64]	**Up to August 2015** **PubMed, Embase, and Web of Science**	**Inclusions:** not specified **Exclusions:** not specified	Highest coffee consumption (varying cut-off)	Lowest coffee consumption (varying cut-off)	CRC risk: 19 case-control or Cohort 2,046,575 individuals and 22,629 cases of CRC	RR=0.98(0.90; 1.06) **Subgroup:** Women RR=0.94(0.79; 1.17) Men: RR=1.01(0.88; 1.17)	Quality: NOS mean=7.6 **Heterogeneity:** P=0.03; I^2=41% **Publication bias:** Begg p=0.94 Egger p=0.76

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
					FU: 4.5 to 18 y		
			Coffee Dose response Incremental of the number cups/day (cp/d)	Non drinkers	CRC	**Dose response** incremental of 4 cp/d RR=0.97(0.92; 1.03) **Cubic spline model** Incremental of 1cp/d RR= 1.00(0.99;1.02) Incremental of 2cp/d RR=1.00(0.97; 1.04) Incremental of 3cp/d RR=1.00(0.96; 1.04) Incremental of 4cp/d RR=0.98(0.96; 1.03) Incremental of 5cp/d RR=0.96(0.91; 1.00) Incremental of 6cp/d **RR=0.93(0.89; 0.99)** Incremental of 7cp/d **RR=0.90(0.85; 0.97)**	**Quality** : not specified for sub-group **Heterogeneity:** P=0.08; I^2=34% **Publication bias:** Begg p=0.77 Egger p=0.43

Study Country (Reference)	**Search period and databases searched**	**Inclusions / exclusions**	**Intervention**	**Control**	**Outcomes**	**Results***	**Quality score Heterogeneity Publication bias**
						Incremental of 8cp/d **RR=0.87(0.80; 0.95)**	
					Colon cancer incidence	RR=0.92(0.83; 1.02)	**Quality** : not specified for sub-group **Heterogeneity:** P=0.12; I^2=30% **Publication bias:** Begg p=0.62 Egger p=0.70
					Rectal cancer incidence	RR=1.06(0.95; 1.19)	**Quality** : not specified for sub-group **Heterogeneity:** P=0.31; I^2=13% **Publication bias:** Begg p=1.00 Egger p=0.82
Vieira et al, 2017* UK [27]	**Up to May 2015**	**Inclusion:** 1) RCT, Cohort or case-control design, 2) report adjusted estimates of the RR and 95% CIs for the association of foods and CRC incidence; 3) for dose–response meta-analysis, studies should provide a quantitative measure of the intake.	Coffee Dose response Incremental of 1 cup/day		CRC risk 14 Cohort	OR=1.00(0.99; 1.02)	***Quality:*** *"high quality"* ***Heterogeneity:*** I^2=44%, p=0.05 **Publication bias** Egger's $p = 0.002$

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
					Colon cancer 11 Cohort	OR=0.99(0.97; 1.01)	**Heterogeneity:** I^2=49%, p=0.03 **Publication bias:** Egger's: p=0.55
					Rectal cancer 15 Cohort	OR=1.01(1.00; 1.03)	**Heterogeneity:** I^2=2%, p=0.43 **Publication bias:** Egger's p=0.73
FISH AND OMEGA-3							
Geelen et al, 2007 Netherlands [65]	**until January 2006**	**Inclusions:** prospective Cohort studies on CRC with data on the exposures ''fish'' or ''n-3 fatty acids''	Highest fish consumption (varying cut-off)	Lowest fish consumption (varying cut-off)	CRC incidence 14 Cohort	RR=0.88(0.78; 1.00) Dose-response: 1 time/week RR=0.96(0.92; 1.00) 100g/week RR=0.97(0.92; 1.03) **Subgroup:** Women: RR=0.78(0.58; 1.06) Men: RR=0.94(0.75; 1.18)	No quality assessment **Heterogeneity:** P=0.25; I^2=18% **Publication bias:** Egger p=0.66
					Colon cancer incidence 8 Cohort	RR=0.87(0.74; 1.02)	**Heterogeneity:** P=0.33; I^2=13%
					Rectal cancer incidence 4 Cohort	RR=0.84(0.55; 1.29)	**Heterogeneity:** P=0.04; I^2=64%

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
Huxley et al., 2009* Australia [34]	**1996-January 2008**	**Inclusions:** 1) published quantitative estimates and standard errors (or some other measure of variability) of the association between each risk factor and 2) CRC **Exclusions:** 1) provided only an estimate of effect, with no means by which to calculate the standard error, or if the estimates were not at least age adjusted	Highest fish consumption (varying cut-off)	Lowest fish consumption (varying cut-off)	CRC risk Unk for fish 5,317 Cases	RR=0.93(0.84; 1.04)	No quality assessment **Heterogeneity:** P=0.25; I^2=18% **Publication bias:** Egger p=0.66
Shen et al., 2012 China [67]	**up to February 2012**	**Inclusions:** prospective Cohort design; the exposure of interest was dietary n-3 fatty acids; the out- come of interest was incidence of colorectal, colon or rectal cancer; risk estimates and associated 95 % CI (or data to calculate them) were provided.	Highest n-3 fatty acid consumption (varying cut-off)	Lowest n-3 fatty acid consumption (varying cut-off)	CRC risk 7Co 4,656 cases/489, 465 patients FU: 6-22 yrs	RR=0.97(0.86; 1.10) <u>Subgroup:</u> Women RR=1.07(0.91; 1.26) Men RR=0.87(0.75; 1.00)	Quality not reported **Heterogeneity:** P=0.09; I^2=38% **Publication bias:** Egger p=0.66 Begg p = 0.76
					Colon cancer risk	RR=0.85(0.72; 1.01)	
					Rectal cancer risk	RR=1.13(0.89; 1.44)	
Wu et al., 2012 China [66]	**Up to May 2012**	**Inclusion:** 1) Cohort or case-control study design, 2) exposure of interest was fresh fish consumption, 3) number of CRC cases and controls had to be reported, 4) RRs or ORs with their corresponding 95% CI for highest versus non/lowest level of fish intake had to be reported.	Fish consumers (varying cut-off)	non/lowest consumers (varying cut-off)	CRC risk 22Co; 19 case-control	**RR=0.87(0.80; 0.95)**	Quality not reported **Heterogeneity:** P<0.01 No publication bias

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
					Colon cancer risk 14 Cohort or case-control	RR=0.96(0.81; 1.14)	Quality not reported **Heterogeneity:** P<0.01 No publication bias
					Rectal cancer risk 7 Cohort or case-control	**RR=0.79(0.65; 0.97)**	Quality not reported **Heterogeneity:** P=0.03 No publication bias
Pham et al., 2013 **Japan** [68]	**Up to November 2012**	**Inclusions:** Only studies on Japanese populations living in Japan were included	Fish consumers (varying cut-off)	Lowest consumers (varying cut-off)	CRC incidence 5Co; 12 case-control	Cohort: OR=1.03(0.89; 1.18) case-control: **OR=0.84(0.75; 0.94)**	Quality not reported **Heterogeneity:** Cohort: P=0.99; I^2=0% case-control: P=0.60; I^2=0% **Publication bias not reported**
					Colon cancer	Cohort: OR=0.96(0.77; 1.21) case-control: **OR=0.84(0.73; 0.98)**	
					Rectal cancer	Cohort: OR=0.96(0.77; 1.21) case-control: **OR=0.83(0.70; 0.99)**	
Yu et al., 2014 **China** [69]	**1945-May 2013**	**Inclusions:** 1) prospective Cohort design; 2) reported RRs or HRs and corresponding 95% CIs (or data to calculate them) of GI cancer relating to different levels of fresh fish intake; and	Fish consumers (varying cut-off)	non/lowest consumers (varying cut-off)	CRC risk 20 Cohort 14,097 cases/ 1,633,066	**RR=0.93(0.87; 0.99)** Incremental estimates for 20g/day of fish	Quality not reported **Heterogeneity:** Cohort: P<0.01;

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
		3) included the frequency of fish consumption			controls Average FU: 13.6 years	consumption: RR=0.99(0.97-1.01)	I^2=65% **No publication bias**
					Colon cancer risk 12 Cohort	**RR=0.95(0.91; 0.98)**	Quality not reported **Heterogeneity:** Cohort: P=0.16; I^2=34%
					Rectal cancer risk 8Co	**RR=0.85(0.75; 0.95)**	Quality not reported **Heterogeneity:** Cohort: P=0.02; I^2=58%
			Low fish consumption (varying cut-off)	non/lowest consumers (varying cut-off)	CRC risk	RR=0.95(0.92; 1.02)	Quality not reported **Heterogeneity:** Cohort: P=0.83; I^2=0%
			High fish consumption (varying cut-off)	non/lowest consumers (varying cut-off)	CRC risk	**RR=0.91(0.82; 0.99)**	Quality not reported **Heterogeneity:** Cohort: P=0.00; I^2=66%
Vieira et al, 2017* UK [27]	**Up to May 2015**	**Inclusion:** 1) RCT, Cohort or case-control design, 2) report adjusted estimates of the RR and 95% CIs for the association of foods and CRC incidence; 3) for dose–response meta-analysis, studies should provide a	Dose response Incremental of 100g/day		CRC risk 11 Cohort or case-control 10,356 cases	**RR=0.89(0.80; 0.99)**	Quality not reported **Heterogeneity:** p=0.52; I^2=0%

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
		quantitative measure of the intake.					**Publication bias:** Egger's p=0.27
					Colon cancer risk 11 Cohort or case-control	RR=0.91(0.80; 1.03)	**Heterogeneity:** Cohort: P=0.76; I^2=0% **Publication bias:** Egger's p=0.32
					Rectal cancer risk 10 Cohort or case-control	RR=0.84(0.69; 1.02)	**Heterogeneity:** Cohort: P=0.31; I^2=15% **Publication bias:** Egger's p=0.56
CALCIUM							
Weingarten et al. 2008 Israel [71]	Up to Dec 2009 Cochrane, MEDLINE, Cancerlit, Embase	**Inclusions:** 1) Supplementation with Ca salts in doses above 1200 mg elemental Ca per day, 2) duration of intervention longer than 6 months **Exclusions:** 1) combined interventions in which there was no arm testing for Ca supplementation alone, observational studies, 2) data from familial polyposis coli **Population:** healthy adults, adults at higher risk of colon cancer due to	Ca salts 1200 mg and 2000mg per day, ≥6months	placebo or no intervention	CRC incidence 2 RCT N=1,346 subjects	OR=0.34(0.05;2.15)	Quality not reported Heterogeneity: I^2 = 0%, p=0.99 Publication bias: Not reported

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
		family history, previous adenomatous polyps, or inflammatory bowel disease are considered.					
Huncharek et al., 2009 USA [73]	Jan1966-Feb 2007 (MEDLARS) Jan 1966-Feb 2003 (Cochrane) MEDLARS, CancerLit, Cochrane database	**Inclusions:** 1) observational studies 2) patients with histologically proven adenocarcinoma of colon/rectum, 3) availability of data on exposures of interest including dairy products, dietary Ca, and/or vit D intake, 4) availability of ORs or RRs with 95% CIs for each report or availability of raw data to calculate these parameters; and availability of data on outcome of interest including incident CRC **Exclusions:** 1) animal studies, 2) in vitro studies, 3) review articles, letters to the editor, 4) abstracts, and non-peer- reviewed articles	Ca supplement (dose threshold varies within studies; ≥500mg/d to ≥700 mg/d)	No Ca supplement dose (<700mg to 0mg/d)	CRC incidence 5 Cohort N=unk	**RR=0.76(0.65;0.89)**	Quality not reported Heterogeneity: P=0.23 Publication bias: None reported
Bristow et al., 2013 New Zealand [72]	1966-2012 Medline, Embase, Cochrane Central	**Inclusion**: 1) RCT, 2) dose ≥500 mg/d of elemental Ca was administered, ≥100 participants randomised; participants of either sex were studied; and the duration of the trial was >1 year **Exclusions:** 1) cohort-administration of Ca and vit D and compared with placebo (studies were eligible if vit D was given to both intervention and control groups), 2) administered in the form of a complex nutritional supplement or as a dietary modification, 3) participants had a major systemic disease other than osteoporosis or colorectal adenoma.	Ca supplements ≥500 mg/d	Placebo	CRC incidence 7 RCTs n=10,496 FU : 3,9yrs Study level, 4 RCT patient level n=7221, FU : 3.5yrs	Study level: RR=1.38(0.89;2.15) Patient level **HR=1.63 (1.01;2.64)**	Quality not reported Heterogeneity: I^2= 0%, Publication bias: no indication of publication bias

Study Country (Reference)	**Search period and databases searched**	**Inclusions / exclusions**	**Intervention**	**Control**	**Outcomes**	**Results***	**Quality score Heterogeneity Publication bias**
Keum et al., 2014 USA [74]	January 1966-Feb 2007 (MEDLARS) Jan 1966-Feb 2003 (Cochrane) MEDLARS, CancerLit, Cochrane database	**Inclusions:** 1) prospective observational study (Cohort studies analyzed with nested case-control, case- cohort, or prospective cohort approaches) **Exclusions:** 1) retrospective studies, 2) non English-language	300 mg/day increase.	Dose response	CRC risk / Dose response 5 Cohort N=920,837	**RR=0.91(0.86;0.98)**	Quality not reported Heterogeneity: I^2 = 67%, p=0.01 Publication bias: Egger =0.43, Begg =0.85
Heine-Bröring et al., 2015* [22]	Up to January 2013 Medline, Embase and Cochrane	**Inclusions:** prospective cohort studies if they reported original and peer-reviewed data on the association of dietary supplement use and colorectal, colon, or rectal cancer incidence. To be included in the meta-analyses, information on ascertainment of colorectal cancer cases, and estimates of the RR 95% CI were required **Exclusions:** studies on colorectal adenomas, RCTs and case-control studies	Ca	No intake	**CRC incidence** 8 Cohort N=unk	**RR=0.86(0.79;0.95)**	Quality performed: none Heterogeneity: I^2=64%; p=0.01 Publication bias: not reported
			Ca increase of 100 mg/d	Control	**CRC incidence** 6 Cohort N=unk	**RR=0.96(0.94;0.99)** Subgroup: Female: RR=0.97(0.94;1.00) Male: RR=0.95(0.95;1.02)	Heterogeneity: I^2=0.77; p<.0.01
VITAMIN A							
Liu et al., 2015 China	Up to April 2014	**Inclusions:** 1) Co studies, 2) the exposure of interest was vitamin or	highest level vitamin	Lowest level of vitamin	CRC incidence	Vit A: RR=0.87(0.75;1.03)	Quality performed:

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
[23]	Pubmed	multiple-vitamin supplement intake, 3) the outcome of interest was the incidence of colorectal, colon, or rectal cancer , 4) RR or OR estimates with 95 % CI were reported; **Exclusions:** Articles with<6 stars			9 Co for Vit A N=unk median 10,000UI/d		NOS (6-8 stars) Heterogeneity: Vit A: I^2 = 0%; Publication bias: Vit A: p=unk
Heine-Bröring et al., 2015 [22]	Up to January 2013 Medline, Embase and Cochrane	**Inclusions:** prospective Cohort studies if they reported original and peer-reviewed data on the association of dietary supplement use and colorectal, colon, or rectal cancer incidence. To be included in the meta-analyses, information on ascertainment of colorectal cancer cases, and estimates of the RR with 95% CI were required **Exclusions:** studies on colorectal adenomas, RCT and case-control studies	Intake of multivitamins, Vit A, Vit C, Vit E, Vit D, Calcium* and Garlic.	No intake	**Colon cancer incidence** 2Co for Vit A 0 vs >5000 and <5000 0 Vs 10000/day (at least 1/week)	Vit A : **RR=0.77(0.62;0.94)**	Quality performed: none Heterogeneity: Vit A: I^2=0%; p=0.76 Publication bias: not reported
			Highest level of multivitamins, Vit A, Vit C, Vit E, Vit D, Ca and Garlic.	Lowest level of multivitamins, Vit A, Vit C, Vit E, Vit D, Ca and Garlic.	**Colon cancer incidence** 2 Cohort for Vit A	Vit A: RR=0.79(0.62;1.01)	Quality performed: none Heterogeneity: Vit A: I^2=0%; p=0.97 Publication bias: not reported
VITAMIN B (FOLIC ACID EXCLUDED)							
Liu et al., 2015 China [23]	Up to April 2014	**Inclusions:** 1) Cohort studies, 2) the exposure of interest was vitamin or multiple-vitamin supplement intake, 3)	highest level vitamin	Lowest level of vitamin	CRC incidence	Vit B2: **RR=0.86(0.76;0.97)**	Quality performed: NOS

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
	Pubmed	the outcome of interest was the incidence of colorectal, colon, or rectal cancer , 4) RR or OR estimates with 95 % CI were reported; **Exclusions:** Articles with<6 stars			5 Cohort for Vit B2 2 Cohort for Vit B3 17 Cohort for Vit B6 12 Cohort for Vit B12 N=unk	Vit B3: RR=1.18(0.76;1.84) Vit B6: **RR=0.88(0.79;0.99)** Vit B12: RR=1.10(0.92;1.32)	Heterogeneity: Vit B2: I^2 = 0%; Vit B3: I^2 = 31%; Vit B12: I^2 = 49%; Vit B6: I^2 = 41%; Publication bias: Vit B2: p=unk Vit B3: p=unk Vit B6: p=0.51 Vit B12: p=unk
Larsson et al., 2010 Sweden [70]	up to Feb 2010 Medline Embase	**Inclusions:** 1) prospective design 2) exposure of interest was intake of vitamin B6 or blood levels of PLP 3) the outcome of interest was colorectal, colon or rectal cancer, and 4) RR estimates with 95%CI or data to calculate these were reported.	dietary vit B6 <Q1 (min 1.02/day) >Q5 max 4.36mg/day. Dietary only except 2 studies dietary and supplements together but none supplements alone	highest vs lowest category	CRC incidence 8 Cohort and 1 nested case-control	Pooled RR=0.90(0.75 ;1.07) Colon RR=0.97(0.81;1.18)	Quality performed NOS Publication bias No evidence Heterogeneity I^2 = 56.2% (95% CI, 0%-76%) P=0.01 Sensivity I^2=24%, p=0.23
STATINS							
Bardou et al., 2010 France [76]	Last 10 years up to September 2009.	**Inclusion:** 1) RCT, case-control and Cohort, 2) assessed or reported colorectal, digestive, gastrointestinal, colon and rectal cancer prevalence in subjects taking, or not taking, statins,	Highest level of Ca	Lowest level of Ca	**CRC incidence** 6 Cohort N=unk	**RR=0.80(0.70;0.92)**	Quality performed: none Heterogeneity: I^2=49%; p=0.08

Study Country (Reference)	**Search period and databases searched**	**Inclusions / exclusions**	**Intervention**	**Control**	**Outcomes**	**Results***	**Quality score Heterogeneity Publication bias**
	EMBASE, MEDLINE, CENTRAL and ISI Web of knowledge	3) articles that contained sufficient detail to reconstruct 2x2 tables **Exclusions:** 1) not published in English or French, 2) without specific cancer site assessment, 3) not assessing digestive tract cancers 4) studies included from the same author					Publication bias: not reported
Bonovas et al., 2007 Greece [78]	Up to December 2006 Medline, Web of science	**Inclusion**: 1) RCT, case-control and Cohort, 2) evaluated exposure to statins and risk of colorectal cancer. RCTs were considered eligible if they evaluated 1) statin therapy compared with placebo or no treatment, 2) no other intervention difference between the experimental and the control group, 3) enrolled at least 2,000 participants, 4) minimum duration of 3 years, 5) reported CRC incidence during the trial. **Exclusions:** 1) insufficient published data for determining an estimate of relative risk (RR) and a CI. Only data from the most recent report were included	Statin Duration>3yrs	Placebo or usual care	CRC incidence 6 RCT, 9CC, 3Co N=55 113 from RCT, 325 000 person-year. N>1.5million from case-control and Cohort of whom 38 124 cancer cases	RCT: RR=0.95(0.81; 1.11), fixed-effects model RR=0.95(0.80; 1.13), random-effects model **case-control and Cohort:** **RR=0.92(0.88; 0.96),** random-effects model **RR=0.92(0.90; 0.95),** fixed-effects model	Quality not reported Heterogeneity: RCT: I^2= 9%, p=0.36 case-control and Cohort: I^2= 16%, p=0.29 Publication bias: RCT: Begg's and Egger's test: p=0.99 and p=0.88 Obs : Begg=0.24 and Egger=0.36
Browning et al., 2007 UK [79]	Up to November 2005 MEDLINE, EMBASE, Web of Science, ISI	**Inclusions: 1)** RCT, case-control and Cohort 2) measured all-cancer or site-specific cancer incidence or fatality associated with statins. 3) A measure of the strength of the association must have been stated in the form of RR or OR, or could be calculated from the raw data presented in the article, 4)	Statin Min FU: 3.6 RCT, 6.2 yrs	Placebo or no treatment	CRC incidence 9 RCT, 3 case-control, 2 Cohort N=103,573	RCT: RR=1.02 (0.89; 1.16) case-control and Cohort: RR=0.84 (0.59; 1.21) Random-	Quality not reported Heterogeneity: RCT I^2=0% case-control and Cohort;: I^2=89%

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
	Proceedings and BIOSIS Previews	statins compared to placebo, 5) observational studies if they compared statins vs. no statins. **Exclusions: 1)** Observational studies that only compared statin use with other lipid lowering agents 2) only highly specific populations, such as renal transplant patients and those with familial hypercholesterolaemia, 3) full-text articles			for RCT for all cancer outcome 826,854 for case-control and Cohort for all cancer outcomes (unk for colorectal)	effects model **RR=0.86(0.77; 0.96)**	Publication bias: Observational: Egger's test, p=0.8
Dale et al., 2006 USA [75]	up to July 2005 Medline, EMBASE, CINAHL, Web of Science, CANCERLIT, the cochrane database	**Inclusions:** 1) RCT 2) statin compared to placebo- or routine treatment, 3) mean (or median) duration of patient follow-up of at least 1 year, 4) enroll a minimum of 100 patients, and 5) report data on the incidence of either cancer diagnosis or cancer death **Exclusions:** not specified	Statin Duration >1yr	Placebo	Colon cancer incidence 4 RCTs N=27,972	RCT: OR=0.95(0.73; 1.25)	Quality not reported Heterogeneity: RCT p= 0.24 Publication bias: Not reported for colon cancer
Kuoppala et al., 2008* Finland [80]	up to October 2007 MEDLINE, EMBASE and Cochrane CENTRAL	**Inclusions:** original study comparing statin treatment with an inactive control (placebo or no statins), adult study participants (18 years or older), cancer incidence reported, and follow-up over 1 year **Exclusions:** Studies on cerivastatin and those describing statin treatment in cancer or transplant patients	Statin	Control	Colon cancer incidence 13 RCT, case-control or Cohort N=31,272	Colorectal RR=0.74(0.47; 1.20) Colon RR=1.00(0.61; 1.70) Rectum: RR=1.10 (0.45; 2.50)	Quality and evidence reported Heterogeneity: Not reported Publication bias: Not reported for colon cancer
Liu et al. 2014 China [81]	Up to July 30, 2013 PubMed,	**Inclusions:** 1) RCT, case-control and Cohort, 2) original studies evaluated exposure to statins and risk of CRC; 3) provided RR estimate (risk ratio, rate	Statin (Long term use and type of statin subgroup	Placebo or no treatment	Colon cancer incidence 11 RCT, 18 case-control,	Overall: **RR=0.90 (0.86; 0.95)** Random-effects model	Quality not reported Heterogeneity:

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
	Embase, Web of Science, and Cochrane library	ratio, HR, or OR) with the corresponding 95 % CIs or sufficient data to calculate them; 4) full-text articles **Exclusions:** (1) did not fulfill the inclusion criteria; (2) reviews, letters, editorials, conference abstracts, or case reports; 3) animal trials.	analysis)		13 Cohort N=95,984 for RCT 7,812,690 for case-control and Cohort	Long term > 5years RR=0.96(0.90; 1.03) RCT: RR=0.96(0.85; 1.08) Random-effects model RR=0.94 (0.86; 1.04) fixed-effects models **case-control and Cohort:** **RR=0.89 (0.84; 0.95)** case-control**:** **RR=0.84(0.76; 0.93)** Cohort: **RR=0.93(0.87; 0.99)** **Lipophilic** RR=**0.88 (0.85; 0.93)**	Overall: I^2= 67%; p <0.01 RCT: I^2=22%; p=0.24 case-control and Cohort: I^2=73%; p < 0.01 case-control: I^2=78%; p<0.01 Cohort: I^2=62%; p<0.01 Publication bias: Begg= 0.42, Egger 0.11
Lytras et al., 2014 Greece [82]	Up to July 2013 MEDLINE	**Inclusions:** 1) RCT, case-control and Cohort, 2) reported estimated measure of effect size (risk ratio, rate ratio, HR or OR) and its associated CI, or had to provide enough data to calculate such an effect measure and CI RCTs were considered eligible if 1) statin was compared with placebo or no treatment; 2) had no other intervention difference between the experimental and the control group; 3) enrolled at	Statin	Placebo or no treatment	Colon cancer risk 8 RCT, 19 case-control, 13 Cohort N Overall >8,2M : 77,994 for RCT, 1.3M for and 7M	Overall: **RR=0.91 (0.87; 0.96)** Random-effects model **RR=0.94 (0.92; 0.96)** fixed-effects models RCT: RR=0.89 (0.74;	Quality not reported Heterogeneity: Overall: I^2=71%, p<0.01 RCT: I^2=25%, p=0.23, Obs I^2=75% p<0.01, Cohort: I^2=83%

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
		least 2000 participants; 4) had a minimum duration of 2 years; and 5) reported the incidence of colorectal cancer in both arms during the trial period. **Exclusions:** none			for Cohort	1.07) Random-effects model RR=0.90 (0.78; 1.04) fixed-effects models case-control and Cohort: **RR=0.92 (0.87; 0.96)** Random-effects model **RR=0.94 (0.92; 0.96)** fixed-effects models case-control: **RR=0.92 (0.87; 0.98)** Random-effects model **RR=0.93 (0.91; 96)** fixed-effects models Cohort: **RR=0.91 (0.83; 1.00)** Random-effects model **RR=0.96 (0.93; 0.99)** fixed-effects models	p<0.01, case-control: I^2=64% p<0.01 Publication bias: Overall: Egger=0.33, Begg=0.11 RCT: Egger=0.22, Begg=0.31 Obs: Egger=0.36, Begg=0.16 case-control: Egger=0.56, Begg=0.22 Cohort: Egger=0.54, Begg=0.27
Taylor et al., 2008 USA [77]	Up to December 2006	**Inclusions:** 1) case-control, 2) assess the association between statins and cancer.	Statin	Any comparisons	Colon cancer* 6 case-control	**OR=0.89 (0.82;0.97)** Random-effects model	Quality not reported Heterogeneity:

Study Country (Reference)	Search period and databases searched	Inclusions / exclusions	Intervention	Control	Outcomes	Results*	Quality score Heterogeneity Publication bias
	Medline, Cumulative Index to Nursing and Allied Health, Excerpta Medica, Web of Science , Scopus and BIOSIS-Biological Abstracts	**Exclusions:** 1) insufficient data for determining both the odds ratio (OR) and the 95% CI. Description of excluded studies in article.			N=100,129 cancer cases (unk for colon cancer)		Not reported for colon cancer Publication bias: Not reported for colon cancer

CI: confidence interval, CRC: colorectal cancer, FU: follow-up, HR: hazard ratio, OR ; odds ratio, RCT: randomized controlled trials, RR : relative risk, unk: unknown

Supplementary Table 4 . Components with increased CRC prevention

Authors Country (Reference)	Search period and databases searched	Inclusion / exclusions	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
MEAT (TOTAL MEAT, RED MEAT, PROCESSED MEAT, POULTRY, ANIMAL FAT AND PROTEIN INTAKE)							
Sandhu et al., 2001 UK [83]	Up to June 1999	**Inclusions:** 1) published and unpublished prospective Cohort that contained risk estimates of CRC associated with meat consumption, 2) eligible outcomes were colon or colorectal cancer incidence or mortality. **Exclusions:** 1) case-control and ecological studies, 2) studies that only classified people as to whether they ate meat or not (level of exposure in the exposed group is not quantified)	Dose response all meat 100g/day		CRC incidence	**OR=1.21(1.10;1.33)**	Quality not reported **Heterogeneity:** p=0.06 publication bias: unable to determine
			Dose response red meat		CRC incidence	**OR=1.30(1.13;1.49)**	Quality not reported

Authors Country (Reference)	Search period and databases searched	Inclusion / exclusions	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
		Definition of meat: A broad definition of "meat" was used, which was taken to include red meat, lamb, beef, pork, and processed meats, such as sausages, meat burgers, ham, bacon and other meat products, but which, where possible, excluded white meat, such as poultry.	100g/day				**Heterogeneity:** p=0.02 publication bias: **Begg p=0.03**
Alexander et al., 2009 USA [84]	up to December 2007	**Inclusions:** 1) epidemiologic Cohort and case-control studies that reported results for the association between animal fat intake and CRC	Highest level animal fat intake	Lowest level animal fat intake	CRC Risk 6 Cohort	SRRE=1.04(0.83;1.31), Dose response 20-g/d increment in animal fat intake and colorectal cancer SRRE=1.02(0.95;1.09) **Subgroup:** Male: SRRE=0.96(0.67;1.38) Female: SRRE=1.10(0.77;1.57)	Quality not reported **Heterogeneity:** p=0.22 Publication bias Begg p=0.35 Egger p=0.42
					Colon cancer 4 Cohort	SRRE=1.11(0.81;1.52)	**Heterogeneity:** p=0.12
					Rectal Cancer 2 Cohort	SRRE=1.34(0.90; 1.98)	**Heterogeneity:** p=0.51
			Highest level protein intake	Lowest level protein intake	CRC Risk 6 Cohort or case-control	SRRE=1.05(0.89; 1.22)	**Heterogeneity:** p=0.55
Huxley et al., 2009* Australia Huxley, [34]	1996 to January 2008	**Inclusions:** 1) published quantitative estimates and standard errors (or some other measure of variability) of the association between each risk factor and colorectal cancer	highest level consumption of red meat	lowest level consumption of red meat	CRC Risk 13,407 cases	**RR=1.21 (1.13; 1.29)**	No quality assessment **Heterogeneity:** p=0.72
					Colon risk	**RR=1.14 (1.02; 1.28)**	
					Rectal risk	**RR=1.28 (1.02; 1.60)**	
			highest level	lowest level	CRC Risk	**RR=1.19 (1.12; 1.27)**	No quality

Authors Country (Reference)	**Search period and databases searched**	**Inclusion / exclusions**	**Intervention**	**Control**	**Outcomes**	**Results**	**Quality score Heterogeneity Publication bias**
		Exclusions: 1) provided only an estimate of effect, with no means by which to calculate the standard error, or 2) if the estimates were not at least age adjusted	consumption of processed meat	consumption of processed meat	26 Cohort 13,471 cases		assessment
					Colon risk	**RR=1.21 (1.08; 1.35)**	**Heterogeneity:** p=0.42
					Rectal risk	RR=1.18 (0.99; 1.41)	
			highest level consumption of poultry	lowest level consumption of poultry	CRC Risk 5,461 cases	RR=0.96 (0.86; 1.08)	No quality assessment
Alexander et al., 2011 USA [85]	Up to June 2009	**Exclusion:** 1) reported data for a broad classification of meat, such as 'total meat' categories, which included poultry or fish, were excluded, 2) information pertaining to processed meat intake constituents of red meat, such as fat or protein from animal sources, heterocyclic amine exposure, cooking practices, or adenomatous polyps were obtained but these analyses were beyond the scope of the present assessment	highest level consumption of red meat	lowest level consumption of red meat	CRC cases 25 Cohort	SRRE=**1.12(1.04;1.21)** Adjusted for 3 factors SRRE=1.08(0.99; 1.18) Dose-response each incremental serving per week **SRRE=1.02(1.00;1.04)** Subgroup: Women SRRE=1.01(0.87;1.17), Men SRRE=**1.21(1.04;1.42).**	**No quality assessment** **Heterogeneity:** p=0.01 **Publication bias** Egger's p=0.97
					Colon cancer 15 Cohort	**RR=1.11 (1.03; 1.19)**	**Heterogeneity:** p=0.79
					Rectal cancer 12 Cohort	SRRE=1.19 (0.97; 1.46)	**Heterogeneity: p<0.01**
Pham et al., 2014 Japan [86]	Up to August 2013	Inclusion: Only studies on Japanese populations living in Japan were included	Total meat		CRC Risk 6 Cohort; 8 case-control	RR=1.06 (0.92; 1.22)	Study quality performed – no change for only high quality study No heterogeneity No publication bias
					Colon risk	RR=1.17 (0.99; 1.39)	
					Rectal risk	RR=0.90 (0.71; 1.14)	

Authors Country (Reference)	Search period and databases searched	Inclusion / exclusions	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
			Red meat		CRC Risk	**RR=1.16 (1.00; 1.34)**	Heterogeneity: p=0.11, I^2=28% **No publication bias**
					Colon risk	**RR=1.21 (1.03; 1.43)**	Heterogeneity: - **No publication bias**
			Processed meat		CRC Risk	**RR=1.17 (1.02; 1.35)**	**Heterogeneity:** p=0.09, I^2=30% **No publication bias**
					Colon cancer	**RR=1.23 (1.03; 1.47)**	**No heterogeneity** **No publication bias**
			Total poultry		Rectal cancer	**RR=0.80 (0.67; 0.96)**	**No heterogeneity** **No publication bias**
Vieira et al, 2017* UK [27]	**Up to May 2015**	**Inclusion:** 1) RCT, Cohort or case-control design, 2) report adjusted estimates of the RR and 95% CIs for the association of foods and CRC incidence; 3) for dose–response meta-analysis, studies should provide a quantitative measure of the intake..	Red and processed meat Dose response Incremental of 100g/day		CRC risk 15 Cohort 10,738 cases	**RR=1.12 (1.04; 1.21)**	Quality not reported **Heterogeneity:** p=0.30; I^2=18% Egger : p= 0.46
					Colon cancer 10 Cohort 10,010 cases	**RR=1.19 (1.10; 1.30)**	**Heterogeneity:** p=0.49; I^2=0% **Egger : p= 0.02**

Authors Country (Reference)	Search period and databases searched	Inclusion / exclusions	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
					Rectal cancer 6 Cohort 3,455 cases	RR=1.17 (0.99; 1.39)	**Heterogeneity:** P<0.01; I^2=91% Egger : p= 0.12
			Red meat Dose response Incremental of 100g/day		CRC risk 8 Cohort 6,662 cases	**RR=1.12 (1.00; 1.25)**	**Heterogeneity:** P=0.24; I^2=23.6% Egger : p= 0.48
					Colon cancer 11 Cohort 4,081 cases	**RR=1.22 (1.06; 1.39)**	**Heterogeneity:** P=0.33; I^2=11.7% Egger : p= 0.76
					Rectal cancer 8 Cohort 1,772 cases	RR=1.13 (0.96; 1.34)	**Heterogeneity:** P=0.52; I^2=0% Egger : p= 0.45
			Processed meat Dose response Incremental of 50g/day		CRC risk 10 Cohort 10,738 cases	**RR=1.18 (1.10; 1.28)**	**Heterogeneity:** P=0.34; I^2=11% Egger : p= 0.29
					Colon cancer 12 Cohort 8,599 cases	**RR=1.23 (1.11; 1.35)**	**Heterogeneity:** P=0.18; I^2=26.2% **Egger : p<0.01**
					Rectal cancer 10 Cohort 3,029 cases	**RR=1.08 (1.00; 1.18)**	**Heterogeneity:** P=0.77; I^2=0% Egger : p= 0.61
			Poultry Dose response Incremental		CRC risk 7 Cohort 3,429 cases	RR=0.81 (0.53; 1.25)	**Heterogeneity:** P=0.05; I^2=48% Egger : p= 0.52

Authors Country (Reference)	Search period and databases searched	Inclusion / exclusions	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
			of 100g/day		Colon cancer 10 Cohort 8,429 cases	RR=0.83 (0.63; 1.11)	**Heterogeneity:** P=0.12; I^2=34.6% Egger : p= 0.08
					Rectal cancer 6 Cohort 3,201 cases	RR=0.86 (0.72;1.01)	**Heterogeneity:** P=0.96; I^2=0% Egger : p= 0.60
Woo et al., 2014 Korea [40]	Up to June 20th, 2014	(1) original articles with a case-control or Codesign; (2) articles reporting on cancer risk and diet in the Korean population; (3) studies reporting adjusted OR or RR with 95% CI for the risk of cancer in subjects with the highest category of food intake compared with those with the lowest food intake; and (4) in cases of multiple publications drawn from studies of the same population, only the most recent study was included.	Highest level of meat consumption	Lowest level of meat consumption	CRC risk 3 studies	**RR=1.25 (1.15; 1.36)**	Quality Not performed Heterogeneity P=0.256, I2=26.7% Publication bias Not performed
ALCOHOL							
Longnecker et al., 1990 USA [87]	From 1966 to March 1989	**Inclusions:** 1) alcohol intake had to have been determined quantitatively by means of personal history; 2) otherwise alcohol consumption was likely to be misclassified, and 3) the association of alcohol consumption with risk of CRC might have been underestimated. **Exclusions:** 1 Unpublished data were not eligible for inclusion in the analysis.	Daily alcohol intake 24g/day		CRC incidence 27 case-control or Cohort	**RR=1.10 (1.05; 1.14)** **Subgroup:** Colorectal women: **RR=1.12 (1.01, 1.23)** Colorectal men: **RR=1.10 (1.04, 1.17)**	**Quality:** Assessed by authors with own scale. Low quality studies may have been taken out of analyses **Heterogeneity:** Present both statistical and clinical

Authors Country (Reference)	**Search period and databases searched**	**Inclusion / exclusions**	**Intervention**	**Control**	**Outcomes**	**Results**	**Quality score Heterogeneity Publication bias**
							Publication bias potential bias present
					Colon cancer incidence 14 case-control or Cohort	**RR=1.10 (1.03; 1.17)**	
					Rectal cancer incidence 14 case-control or Cohort	**RR=1.10 (1.02; 1.18)**	
Corrao et al., 1999 Italy [88]	From 1966 to 1998	**Inclusions:** 1) case-control or Cohort published as an original article, 2) findings expressed directly as OR or RR considering three or more levels of alcohol consumption; 3) reported number of cases and non-cases and estimates of the OR or RR for each exposure level. **Exclusions:** 1) ecological and prevalence studies and/or abstracts, letters and editorials	Daily alcohol intake 25g/day 50g/day 100g/day		Colon cancer incidence 12CC and 4 Cohort 5360 Cases	case-control: 25g/day: RR=1.0 (1.0; 1.1) 50g/day **RR=1.10 (1.00; 1.20)** 100g/day **RR=1.10 (1.00; 1.30)** Cohort: 25g/day: **RR=1.40 (1.10; 1.70)** 50g/day **RR=1.90 (1.3; 2.9)** 100g/day **RR=3.6 (1.6; 8.5)**	**Quality:** Mean author score (range): 14 (9; 19) **Heterogeneity:** p<0.01 **Publication bias** funnel plot
					Rectal cancer incidence 11CC and 3 Cohort 2759 Cases	<u>Men</u> 25g/day: RR=1.0 (1.0; 1.2) 50g/day **RR=1.2 (1.1; 1.5)** 100g/day **RR=1.5 (1.2; 2.2)**	**Quality:** Mean author score (range): 13 (9; 19) **Heterogeneity:** p<0.01

Authors Country (Reference)	**Search period and databases searched**	**Inclusion / exclusions**	**Intervention**	**Control**	**Outcomes**	**Results**	**Quality score Heterogeneity Publication bias**
						Women 25g/day: **RR=2.3 (1.3; 4.0)** 50g/day **RR=5.0 (1.6; 16.4)** 100g/day **RR=25.7 (2.5; 267.6)**	**Publication bias** funnel plot
Bagnardi et al., 2001 Italy [89]	From 1966 to 2000	**Inclusions: 1**) case-control or Cohort study published as an original article; 2) OR or RR, considering at least 3 levels of alcohol consumption; 3) papers reporting the number of cases and non-cases, and the estimates of the OR or RR for each exposure level	Daily alcohol intake 25g/day 50g/day 100g/day		*CRC incidence **6 Cohort and 16 case-control**	case-control or Cohort: 25g/day: **RR=1.08 (1.06, 1.10)** 50g/day **RR=1.18 (1.14, 1.22)** 100g/day **RR=1.38 (1.29, 1.49)**	Quality not reported **Heterogeneity:** p<0.05 **Publication bias not reported**
Moskal et al., 2007 France [90]	From 1990 to June 2005	**Inclusions:** 1) prospective Cohort evaluating the relationship between total alcohol consumption and CRC risk; 2) published in English 3) CRC incidence as endpoint; 4) providing RR estimates and its corresponding 95% CI, or information allowing us to compute unadjusted variance. **Exclusions:** Studies in particular populations (i.e. cohorts of alcoholics or brewery workers) were not included.	Highest level of alcohol intake	Lowest level of alcohol intake	Colorectal cancer incidence 7 Cohort	RR=1.34 (0.92; 1.96) **Subgroup:** Colorectal women: RR= 0.88 (0.61; 1.27) Colorectal men: RR= 1.73 (1.00; 2.98)	Quality not reported **Heterogeneity:** p<0.01; I^2=71% **Publication bias** Egger's p=0.35 Begg's p=0.88
					Colon cancer incidence 17 Cohort	**RR=1.50 (1.25; 1.79)** **Subgroup:** women: RR= 1.23 (0.97; 1.83) men: **RR= 1.64 (1.39; 1.93)**	Quality not reported **Heterogeneity:** P=0.03; I^2=43% **Publication bias** Egger's p=0.70 Begg's p=0.25

Authors Country (Reference)	Search period and databases searched	Inclusion / exclusions	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
					Rectal cancer incidence 14 Cohort	**RR=1.63 (1.35; 1.97)** **Subgroup:** women: RR=1.39 (0.95; 2.02) men: **RR=1.79 (1.38; 2.33)**	Quality not reported **Heterogeneity:** P=0.68; I^2=0% **Publication bias** Egger's p=0.70 Begg's p=0.34
			Daily alcohol intake 25g/day 50g/day 100g/day		Colon cancer incidence	25g/day: **RR=1.03 (1.02; 1.05)** 50g/day **RR=1.07 (1.03; 1.11)** 100g/day **RR=1.15 (1.07; 1.23)**	
					Rectal cancer incidence	25g/day: **RR=1.04 (1.02; 1.05)** 50g/day **RR=1.07 (1.05; 1.10)** 100g/day **RR=1.15 (1.10; 1.21)**	
Fedirko et al., 2011 USA [91]	Up to May 2010	Inclusions: 1) case-control or Cohort, 2) alcohol intake and CRC incidence or mortality in general population, 3) reporting the OR or RR estimates with the corresponding 95% CI or sufficient information to calculate them; 4) reporting an association for at least three categories of alcohol consumption.	Drinkers	Non-occasional drinkers	CRC incidence 23 Cohort and 34 case-control	**RR=1.12 (1.06; 1.19)** **Subgroup:** Colorectal women: RR=1.00 (0.94; 1.07) Colorectal men: **RR=1.25 (1.13; 1.39)**	**Quality:** authors criteria **Heterogeneity:** potential heterogeneity of effects by sex, colorectal site, **Publication bias** minor evidence of publication bias.

Authors Country (Reference)	Search period and databases searched	Inclusion / exclusions	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
					Colon cancer incidence 42 Cohort or case-control	RR=1.05 (0.99; 1.12)	
					Rectal cancer incidence 38 Cohort or case-control	**RR=1.19 (1.09; 1.31)**	
			Light alcohol intake (≤1 drink/ day (≤12.5 g/day of ethanol))	Non-occasional drinkers	CRC incidence 23 Cohort and 26 case-control	RR=1.00 (0.95; 1.05) **Subgroup:** Colorectal women: RR=0.95 (0.89; 1.01) Colorectal men: RR=1.02 (0.92; 1.14)	
					Colon cancer incidence 36 Cohort or case-control	RR=0.96 (0.90; 1.02)	
					Rectal cancer incidence 32 Cohort or case-control	RR=1.06 (0.98; 1.14)	
			Moderate alcohol intake (2–3 drinks/day (12.6–49.9 g/day of ethanol))	Non-occasional drinkers	CRC incidence 22 Cohort and 31 case-control	**RR=1.21 (1.13; 1.28)** **Subgroup:** Colorectal women: **RR=1.08 (1.03; 1.13)** Colorectal men: **RR=1.24 (1.13; 1.37)**	
					Colon cancer incidence 39 Cohort or case-control	**RR=1.15 (1.06; 1.24)**	
					Rectal cancer incidence	**RR=1.23 (1.13; 1.35)**	

Authors Country (Reference)	**Search period and databases searched**	**Inclusion / exclusions**	**Intervention**	**Control**	**Outcomes**	**Results**	**Quality score Heterogeneity Publication bias**
					35 Cohort or case-control		
			Heavy alcohol intake (≥4 drinks/day (≥50 g/day of ethanol))	Non-occasional drinkers	CRC incidence 7 Cohort and 12 case-control	**RR=1.52 (1.27; 1.81)** **Subgroup:** Colorectal women: **RR=1.54 (1.04; 2.29)** Colorectal men: **RR=1.62 (1.31; 2.01)**	
					Colon cancer incidence 16 Cohort or case-control	**RR=1.43 (1.23; 1.67)**	
					Rectal cancer incidence 15 Cohort or case-control	**RR=1.59 (1.18; 2.15)**	
Bagnardi et al., 2013 Italy [92]	Up to December 2010	Inclusion: 1) case-control or Cohort published as original articles, 2) OR, RR or HR (or reporting sufficient data to compute them) for 3) light drinkers (≤12.5 g ethanol; ≤1 drink) versus non-drinkers. 4) studies that reported standard errors or CIs of the risk estimates, or provided sufficient data to calculate them. Exclusions: 1) abstracts, letters, reviews and meta-analyses, 2) Specific type of alcoholic beverage only (e.g. beer only)	Light drinkers (≤12.5 g ethanol; ≤1 drink)	Non-drinkers	*CRC incidence 26 Cohort, 28 case-control	**case-control or Cohort:** RR=0.99 (0.95; 1.04) **Cohort:** RR=1.00 (0.95, 1.05) **case-control:** RR=0.98 (0.91, 1.06) **Subgroup:** Colorectal women: RR= 0.93 (0.87, 0.99) Colorectal men: RR= 1.05 (0.95, 1.16)	Quality not reported **Heterogeneity:** Moderate or low **Publication bias:** P=0.059
Bagnardi et al., 2015 Italy [93]	Up to September 2012	**Inclusion:** 1) case-control or Cohort published as original articles, 2) reported OR, RR or HR (or reporting sufficient data to compute them) for 3) light drinkers (≤12.5 g ethanol; ≤1 drink) versus non-drinkers. 4) studies that	Daily alcohol intake ≤12.5g/day ≤50g/day >50g/day		*CRC **33 Cohort and 33 case-control**	case-control or Cohort: ≤12.5g/day RR=0.99 (0.95; 1.06) ≤50g/day **RR=1.17 (1.11, 1.24)** >50g/day	Quality not reported **Heterogeneity:** ≤12.5g/day;

Authors Country (Reference)	Search period and databases searched	Inclusion / exclusions	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
		reported standard errors or CIs of the risk estimates, or provided sufficient data to calculate them. **Exclusions:** 1) abstracts, letters, reviews and meta-analyses, 2) Specific type of alcoholic beverage only (e.g. beer only)				**RR=1.44 (1.25, 1.65)** **Subgroup:** Colorectal women: ≤12.5g/day: RR= 0.95 (0.89; 1.01) ≤50g/day: RR=1.07 (0.99; 1.16) >50g/day: RR=1.24 (0.68; 2.25) Colorectal men: ≤12.5g/day: RR= 1.05 (0.95; 1.16) ≤50g/day: **RR=1.21 (1.11; 1.32)** >50g/day: **RR=1.53 (1.30; 1.80)**	I^2=40 ≤50g/day: I^2=52 >50g/day: I^2=69 **Publication bias not reported**
Wang et al., 2015 USA [94]	Up to July 2014	**Inclusions:** 1) case-control or Cohort, 2) alcohol intake and CRC incidence or mortality in general population, 3) reporting the OR or RR estimates with the corresponding 95% CI or sufficient information to calculate them; 4) reporting an association for at least three categories of alcohol consumption	Drinkers	Non- or occasional drinkers	CRC incidence 22 Cohort and 2 case-control	**RR=1.13 (1.09; 1.17)** **Subgroup:** Colorectal women: RR=1.03 (0.95; 1.10) Colorectal men: **RR=1.19 (1.07; 1.32)**	**Quality:** authors criteria **Heterogeneity:** Colorectal heterogeneity **Publication bias** Significant publication bias
					Colon cancer incidence 6 Cohort or case-control	**RR=1.18 (1.08; 1.30)**	
					Rectal cancer incidence 3 Cohort or case-control	**RR=1.42 (1.03; 1.98)**	
			Light alcohol intake	Non- or occasional drinkers	CRC incidence 21 Cohort	**RR=1.07 (1.02; 1.13)** **Subgroup:**	

Authors Country (Reference)	Search period and databases searched	Inclusion / exclusions	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
			(≤1 drink/ day (≤12.5 g/day of ethanol))		and 2 case-control	Colorectal women: RR=0.98 (0.91; 1.08) Colorectal men: RR=0.97 (0.88; 1.10)	
					Colon cancer incidence 21 Cohort or case-control	RR=1.02 (0.91; 1.14)	
					Rectal cancer incidence 2 Cohort or case-control	RR=1.28 (0.83; 1.98)	
			Moderate alcohol intake (2–3 drinks/day (12.6–49.9 g/day of ethanol))	Non- or occasional drinkers	CRC incidence 18 Cohort and 2 case-control	**RR=1.23 (1.15; 1.33)** **Subgroup:** Colorectal women: **RR=1.14 (1.04; 1.25)** Colorectal men: **RR=1.28 (1.15; 1.44)**	
					Colon cancer incidence 8 Cohort or case-control	**RR=1.35 (1.21; 1.50)**	
					Rectal cancer incidence 3 Cohort or case-control	RR=1.41 (0.95; 2.08)	
			Heavy alcohol intake (≥4 drinks/day (≥50 g/day of ethanol)	Non- or occasional drinkers	CRC incidence 7 Cohort and 12 case-control	**RR=1.37 (1.28; 1.49)** **Subgroup:** Colorectal women: RR=0.85 (0.84; 1.42) Colorectal men: **RR=1.38 (1.22; 1.57)**	
					Colon cancer incidence 4 Cohort or	**RR=1.23 (1.03; 1.47)**	

Authors Country (Reference)	Search period and databases searched	Inclusion / exclusions	Intervention	Control	Outcomes	Results	Quality score Heterogeneity Publication bias
					case-control		
					Rectal cancer incidence 2 Cohort or case-control	**RR=1.77 (1.09; 2.88)**	
Zhang et al., 2015 China [95]		Inclusions: (1) case-control or Cohort as published as original article; 2) reported RR estimates and corresponding 95 % CI for consumption of beer and CRC incidence at least; adjusted or matched for age	Beer drinker	non-/occasional drinkers	CRC incidence 9 Cohort and 12 case-control	**RR=1.20 (1.06; 1.37)** **Subgroup:** Colorectal women: RR=0.96 (0.69; 1.33) Colorectal men: RR=1.15 (0.66; 2.03)	**Quality:** authors criteria **Heterogeneity:** $p<0.01$; $I^2=73\%$ **Publication bias** Begg's p=0.72 Egger's p=0.75
			Light beer intake (<1 drink or 13g/day)	non-/occasional drinkers	CRC incidence	RR=1.03 (0.95; 1.11)	**Quality:** authors criteria **Heterogeneity:** none **Publication bias** Not reported
			Moderate beer intake (1-2 drinks or 13-26g/day)	non-/occasional drinkers	CRC incidence	RR= 1.09 (0.91; 1.31)	
			Heavy beer intake (>2 drinks or > 26g /day)	non-/occasional drinkers	CRC incidence	**RR=1.37 (1.26; 1.49)**	

CI: confidence interval, CRC: colorectal cancer, HR: hazard ratio, OR ; odds ratio, RCT: randomized controlled trials, RR : relative risk, SRRE : summary relative risk estimate