Supplementary material, Appendix 1 Supplementary methods – details of search strategy
Medline and Embase search through Ovid:
Separate searches were conducted for each dietary component using Ovid MEDLINE® and Embase
Cruciferous vegetables:

1. Colorectal Neoplasms/exp
2. ((colorectal* or rect* or anal* or anus or colon* or sigmoid) adj3 (cancer* or carcinoma or tumo?r* or neoplas* or adenoma or adenocarcinoma))). Ab, kf, ot, ti, tw
3. 1 OR 2
4. (incidence or prevalence or relaps* or prognosis or mortality or morbidity or survival or carcinogen* or chemotherapy* or response or adjuvant or adjunct or chemoprevent* or radiotherapy* or chemoradiotherapy* or risk or odds ratio or hazard ratio). Ab, kf, ot, ti, tw
5. (Cruciferae or Brassicacea? or Brassica? Or cruciferous vegetable* or broccoli or cabbage or cauliflower of (brussel adj1 sprout*) or (mustard adj1 plant*) or sauerkraut or cole (adj1slaw) or collard* of (bok adj1 choy) or (turnip adj1 green*) or raddish). Ab, kf, ot, ti, tw
6. 3 AND 4 AND 5

Citrus fruits:

1. Colorectal Neoplasms/exp
2. ((colorectal* or rect* or anal* or anus or colon* or sigmoid) adj3 (cancer* or carcinoma or tumo?r* or neoplas* or adenoma or adenocarcinoma))). Ab, kf, ot, ti, tw
3. 1 OR 2
4. (incidence or prevalence or relaps* or prognosis or mortality or morbidity or survival or carcinogen* or chemotherapy* or response or adjuvant or adjunct or chemoprevent* or radiotherapy* or chemoradiotherapy* or risk or odds ratio or hazard ratio). Ab, kf, ot, ti, tw
5. (citrus fruit* or lemon* or lime* or orange* or grapefruit* or mandarin* or citron). Ab, kf, ot, ti, tw
6. 3 AND 4 AND 5

Garlic:

1. Colorectal Neoplasms/exp
2. ((colorectal* or rect* or anal* or anus or colon* or sigmoid) adj3 (cancer* or carcinoma or tumo?r* or neoplas* or adenoma or adenocarcinoma))). Ab, kf, ot, ti, tw
3. 1 OR 2
4. (incidence or prevalence or relaps* or prognosis or mortality or morbidity or survival or carcinogen* or chemotherapy* or response or adjuvant or adjunct or chemoprevent* or radiotherapy* or chemoradiotherapy* or risk or odds ratio or hazard ratio). Ab, kf, ot, ti, tw
5. (garlic). Ab, kf, ot, ti, tw
6. 3 AND 4 AND 5

Tomatoes:

1. Colorectal Neoplasms/exp
2. ((colorectal* or rect* or anal* or anus or colon* or sigmoid) adj3 (cancer* or carcinoma or tumo?r* or neoplas* or adenoma or adenocarcinoma))). Ab, kf, ot, ti, tw
3. 1 OR 2
4. (incidence or prevalence or relaps* or prognosis or mortality or morbidity or survival or carcinogen* or chemotherapy* or response or adjuvant or adjunct or chemoprevent* or radiotherapy* or chemoradiotherapy* or risk or odds ratio or hazard ratio). Ab, kf, ot, ti, tw
5. (tomato*). Ab, kf, ot, ti, tw
6. 3 AND 4 AND 5

Nuts:

1. Colorectal Neoplasms/exp
2. ((colorectal* or rect* or anal* or anus or colon* or sigmoid) adj3 (cancer* or carcinoma or tumo?r* or neoplas* or adenoma or adenocarcinoma))). Ab, kf, ot, ti, tw
3. 1 OR 2
4. (incidence or prevalence or relaps* or prognosis or mortality or morbidity or survival or carcinogen* or chemotherapy* or response or adjuvant or adjunct or chemoprevent* or radiotherapy* or chemoradiotherapy* or risk or odds ratio or hazard ratio). Ab, kf, ot, ti, tw
5. (nut or nuts or peanut*). Ab, kf, ot, ti, tw
6. 3 AND 4 AND 5

Supplementary material, Appendix 2 Supplementary methods - gene set enrichment analysis

To investigate potential anticarcinogenic mechanisms of food items, we build a profile of gene/protein perturbations caused by active compounds within each food item and found the most influential gene sets using gene set enrichment analyses.

To build profiles of food items, we use a comprehensive list of predicted anticarcinogenic food compounds published by Veselkov et al [17]. In this work, the authors used a machine learning approach to simulate the effects of FDA-approved drugs on the human protein-protein interaction (PPI) network and trained a model to predict food compounds with anticarcinogenic properties based on their similarity to FDA-approved anticancer drugs at the genome level.

With the list of anticarcinogenic compounds present in each food item (Supplementary Table 2), we built the genomic perturbation profile of each food item as the average of the genomic perturbation profiles of individual compounds in each of them.

Genomic perturbation profiles of individual food compounds were obtained by applying Random Walk with Restarts (RWR), an algorithm which has been termed an ‘amplifier’ of genetic associations [90], to simulate the effect of food compounds on the PPI network given their targets on the PPI. In short, starting from a given food compound’s targets on the PPI network, encoded as binary node features, RWR simulates the overall effect of the said food compound on the PPI, outputting a ‘simulated’ profile: a vector of float values, one value per protein/gene, representing the extent to which proteins/genes are 'affected' or 'perturbed' by the food compound given the initial set of genes perturbed (compound’s targets) and the underlying connectivity of the PPI network.

To find optimal hyperparameters for the RWR algorithm (thresholds for protein-protein connections, threshold for food compound-protein connections, and restart probability for the RWR propagation), we replicated the analysis done by Veselkov et al. [17], building a classifier to predict FDA-approved anticancer drugs based on drugs’ effects on the PPI network. However, we introduced a colorectal cancer-specific component in the model by slightly modifying the input features to the model. Instead of using drug simulated profiles only, as Veselkov et al. did, we used 1-dimensional Pearson correlation values between drug simulated profiles and a colorectal cancer simulated profile as input features. Hence, in the classification task, each sample would correspond to the 1-dimensional Pearson correlation between the drug profile and the colorectal cancer profile.

The cancer profile was formed of multiple colorectal cancer tissue samples. Drug-cancer sample correlations were combined for each drug and available colorectal cancer samples using an aggregation function (e.g. median value or mean value normalized to the standard deviation) to yield a single float value per drug, suitable for simple thresholding for the classification task. We used stratified K-fold (5-fold split with reshuffling, 5 cycles) to find the best propagation parameters and estimate balanced classification accuracy.

The human PPI network and initial binary vectors of food compounds were provided by Veselkov et al. [17]. Colorectal cancer binary gene/protein perturbation profiles were obtained from COSMIC. Drug binary profiles were provided by Veselkov et al. [17]. Classification labels of drugs were also provided by Veselkov et at.[17], the positive class corresponding to the known anticancer drugs and negative class to drugs which had no indication of potential anticancer activity.

Pathway analytics of food item profiles was performed using Gene Set Enrichment Analysis v4.0.3 via the command line. Propagated gene/protein perturbation values were supplied as the input data for “GSEAPreranked” module. Biocarta v7.1 and KEGG v7.1 gene sets were used by default. Functional classification and pathway enrichment analyses were done using PANTHER [27].

Supplementary Table 1 Descriptive characteristics of included case-control studies

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of controls	Number of cases	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
Annema et al., 2011 [42]	Case-Control	Age 40-79 Mixed gender Australia	Tomatoes	FFQ	All Colorectal cancers	939	834	≥0.78 vs <0.21 servings per day	0.96 (0.71-1.29)	sex, age, BMI at age 20y, energy intake, multivitamin use, alcohol consumption, physical activity, smoking, diabetes, socioeconomic status	7
			Citrus fruits					≥0.5 vs <.07 servings per day	0.95 (0.72-1.25)		
			Garlic					≥0.28 vs <.02 servings per day	0.86 (0.68-1.09)		
			Cruciferous vegetables (cabbage, brussels sprouts, cauliflower, broccoli)					≥1.06 vs <.35 servings per day	0.80 (0.6-1.06)		
Franceschi et al., 1998 [48]	Case-Control	Mixed gender Italy	Tomatoes	FFQ Interviews	Colon cancer	5155 2073 males (40%) 3082 females (60%)	1225 688 males (56%) 537 females (44%)	Consumers vs non-consumers	0.9 (0.8-1.0)	age, sex, study center, year of interview, education, physical activity level, intake of alcohol, total energy, parity	6
					Rectal cancer		728 437 males (60%) 291 females (40%)		0.9 (0.8-1.1)		
			Citrus fruits		Colon cancer		1225 688 males (56%) 537 females (44%)		1.0 (0.9-1.1)		
					Rectal cancer		728 437 males (60%) 291 females (40%)		0.8 (0.7-1.0)		
			Garlic		Colon cancer		1225 688 males (56%) 537 females (44%)		0.9 (0.8-1.0)		
					Rectal cancer		728 437 males (60%) 291 females (40%)		0.9 (0.8-1.0)		
			Cruciferous vegetables		Colon cancer		1225 688 males (56%) 537 females (44%)		0.9 (0.7-1.0)		
					Rectal cancer		728 437 males (60%) 291 females (40%)		1.1 (0.9-1.3)		

[a] odds ratio
[b] relative risk
[c] 95% confidence interval
[d] Newcastle-Ottawa Scale

Supplementary Table 1 Descriptive characteristics of included case-control studies (continued)

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of controls	Number of cases	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
Le Marchand et al., 1997 [33]	Case-Control	Males Hawaii	Tomatoes	FFQ Interviews	All Colorectal cancers	698	698	Highest vs lowest quartile	0.8 (0.5-1.2)	caloric intake, age, family history of CRC, alcoholic drinks per week, pack-years of cigarette smoking, lifetime recreational activity, quetelet index 5, total calories, egg, calcium intake	8
			Citrus fruits						0.9 (0.6-1.3)		
			Garlic						0.7 (0.5-1.1)		
			Cruciferous vegetables						0.9 (0.6-1.3)		
		Females Hawaii	Tomatoes			494	494		0.9 (0.5-1.4)		
			Citrus fruits						0.9 (0.6-1.4)		
			Garlic						0.7 (0.5-1.2)		
			Cruciferous vegetables						0.8 (0.5-1.4)		
Abu Mweis et al., 2015 [34]	Case-Control	Age >18 Mixed gender Jordan	Tomatoes	FFQ Interviews	All Colorectal cancers	240 108 males (45%) 132 females (55%)	167 79 males (47%) 88 females (53%)	>3 vs <2 portions per week	0.57 (0.32-1.0)	age, sex, total energy, metabolic equivalent (min/week), smoking, education level, marital status, work income, family history of CRC	7
			Cruciferous vegetables (cauliflower)					weekly vs <1 portion per week	1.15 (0.67-1.97)		
Hu et al., 2007 [43]	Case-Control	Males Canada	Tomatoes	FFQ	Rectal cancer	1635	830	Highest vs lowest quartile	0.9 (0.6-1.4)	education, BMI, total energy intake for both sexes, alcohol use, smoking status for male rectal cancer cases only, age group, province.	8
			Cruciferous vegetables						0.9 (0.5-1.3)		
		Females Canada	Tomatoes			1462	550		1 (0.6-1.5)		
			Cruciferous vegetables						0.6 (0.4-0.8)		
Seow et al., 2002 [44]	Case-Control	Mixed gender Singapore Chinese	Tomatoes	FFQ Interviews	All Colorectal cancers	222 89 males (40%) 133 females (60%)	121 56 males (46%) 65 females (54%)	≥ 365 vs <24 portions per year	1 (0.5-1.7)	age, family history of CRC, gender, smoking history (ever smoked of never smoked), years of formal education, usual number of hours of moderate/vigorous exercise per week	6
			Cruciferous vegetables					≥ 234 vs <234 portions per year	1.3 (0.7-2.3)		

Supplementary Table 1 Descriptive characteristics of included case-control studies (continued)

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of controls	Number of cases	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
Tayyem et al., 2018 [68]	Case-Control	Mixed gender Jordan	Tomato sauce	FFQ	All Colorectal cancers	281	220	daily vs less than monthly	0.44 (0.13-1.57)	Total energy, fruit and vegetable intake, physical activity, smoking, education level, marital status, work status, income, other health problems, CRC history	6
			Fresh tomato juice					weekly vs less than monthly	0.52 (0.15-1.74)		
Fernandez et al., 1997 [63]	Case-Control	Age <75 Family histroy of colorectal cancer Mixed gender Italy	Tomatoes	Interviews	All Colorectal cancers	108	112	high vs low intake	0.2 (0.1-0.4)	Sex, age, area of residence	7
			Citrus fruits						0.4 (0.1-1.1)		
La Vecchia et al., 2002 [69]	Case-Control	Mixed gender Italy	Tomatoes	FFQ Interviews	All Colorectal cancers	4154	1553	Highest vs lowest quintile	0.8 (0.6-0.9)	age, sex, BMI, total calories, physical exercise	6
Deneo-Pellegrini et al., 2002 [35]	Case-Control	Mixed gender Uruguay	Citrus fruits	FFQ Interviews	All Colorectal cancers	1452 882 males (61%) 570 females (39%)	484 294 males (61%) 190 females (39%)	Highest vs lowest quartile	0.8 (0.6-1.1)	age, sex, residence, urban/rural status	7
			Cruciferous vegetables						1.2 (0.8-1.6)		
Levi et al., 1999 [61]	Case-Control	Aged 27-74 Mixed gender Switzerland	Citrus fruits	FFQ	All Colorectal cancers	491 211 males (43%) 280 females (57%)	223 142 males (64%) 81 females (36%)	>3.5 vs 0-1.5 servings per week	0.52 (0.48-0.33)	age, sex, education, smoking, alcohol, BMI, physical activity, total energy intake, meat & vegetable consumption	7
			Garlic					3 vs 1 servings per week	0.39 (0.21-0.7)		
Foschi et al., 2010 [62]	Case-Control	Mixed gender Switzerland	Citrus fruits	FFQ	All Colorectal cancers	6804 3602 males (53%) 3202 females (47%)	3634 2040 males (56%) 1594 females (44%)	≥4 vs <1 portions per week	0.82 (0.74-0.72)	sex, age, study center, tobacco smoking, alcohol, education, BMI, physical activity, energy index	6
Hu et al., 1991 [67]	Case-Control	Hospitalised patients Mixed gender China	Garlic	FFQ Interviews	Rectal cancer	336	336	Consumers vs non-consumers	4.82 (1.19-19.45)		6

Supplementary Table 1 Descriptive characteristics of included case-control studies (continued)

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of controls	Number of cases	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
Galeon et al., 2006 [64]	Case-Control	Age <80 Mixed gender Italy	Garlic	FFQ Interviews	All Colorectal cancers	4765	2280	high vs low intake	0.74 (0.63-0.86)	Energy intake, age, sex, study center, education, BMI, energy intake, alcohol consumption , smoking habit, physical activity	7
Lee et al., 2018 [70]	Case-Control	Mixed gender Korea	Nuts (peanuts, pinenuts, almonds)	FFQ	All Colorectal cancers	1846 1250 males (68%) 596 females (32%)	923 625 males (68%) 298 females (32%)	>45 vs 0 grams per week	0.3 (0.2-0.45)	Age	7
Chun et al., 2015 [72]	Case-Control	Mixed gender Korea	Nuts & legummes	FFQ Interviews	All Colorectal cancers	116 71 males (61%) 45 females (39%)	150 94 males (63%) 56 females (37%)	>10.9 vs <5.24 servings per week	1.35 (0.61-3.01)	Energy intake, sex, age, household income, education, smoking, slcohol drinking frequency, exercide frequency, BMI, dietary fiber, red meat intake	7
Young & Wolf, 1988 [28]	Case-Control	Age 18-35 White Mixed gender USA	Nuts (peanut butter)	FFQ	Colon cancer	618	353	20 vs 1 portion per month	0.33 (0.12-0.89	Age, sex, age x sex	7
			Cruciferous vegeatbles (broccoli, cauliflower, brussels sprouts, turnips)					8 vs 1 portion per month	0.54 (0.36-0.77)		
		Age >35 White Mixed gender USA	Nuts (peanut butter)					20 vs 1 portion per month	1.04 (0.93-1.08)		
			Cruciferous vegeatbles (broccoli, cauliflower, brussels sprouts, turnips)					8 vs 1 portion per month	0.59 (0.41-0.85)		
Evans et al., 2002 [40]	Case-Control	Mixed gender UK	Nuts (peanuts)	FFQ	All Colorectal cancers	512	512	>1 vs <1 serving per week	1.37 (1.01-1.85)	Energy, red meat, alcohol, calcium, protein and fat intake, regular aspirin useage, exercise	9
			Cruciferous vegetables (broccoli)						0.67 (0.45-1.0)		

Supplementary Table 1 Descriptive characteristics of included case-control studies (continued)

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of controls	Number of cases	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
Fang et al., 2019 [29]	Case-Control	Age >18 Mixed gender China	Cruciferous vegetables (greens, cabbage, chinese cabbage, cauliflower, raddish)	Interviews Questionnaires	All Colorectal cancers	1666 966 males (58%) 700 females (42%)	833	Highest vs lowest quartile	0.83 (0.59-1.18)	BMI, colon cancer history in first degree relatives, smoking status, alcohol drinking statu, total energy, red meat intake, total noncruciferous vegetable intake, total fruit intake, consunmption of fried food, cured food, hot and psicy food	7
Steinmetz et al., 1993 [30]	Case-Control	Age 30-74 Mixed gender Australia	Cruciferous vegetables (coleslaw, cooked cabbage, brussels sprouts, cooked broccoli, raw broccoli, cooked cauliflower, other root vegetables)	FFQ Interviews	Colon cancer	438 241 males (55%) 197 females (45%)	220 121 males (55%) 99 females (45%)	>5.8 vs <1.7 servings per week	1.1 (0.57-2.14)	Protein intake, occupation, quetelet's index, alcohol intake	8
Tayyem et al., 2014 [31]	Case-Control	Age >18 Mixed gender Jordan	Cruciferous vegetables (cabbage)	FFQ Interviews	All Colorectal cancers	281	220	Daily vs rarely	2.3 (0.28-19.14)	Age, sex, total energy, MET minutes/weeks, tobacco use, education level, marital status, work, income, family history of CRC	7
			Cruciferous vegetables (Cauliflower)						4.46 (0.72-27.68)		
			Cruciferous vegetables (Broccoli)						1.01 (0.13-7.87)		
Chiu et al., 2003 [32]	Case-Control	Age 30-74 Mixed gender Shanghai, China	Cruciferous vegetables (shanghai bok choi, cabbage, Chinese cabbage, cauliflower)	FFQ Interviews	Colon cancer	1551 851 males (55%) 701 females (45%)	931 462 males (50%) 469 females (50%)	25.4 vs <15 portions per week	0.7 (0.5-1.0)	Age, total energy, education, BMI, income, occupational physical activity	8
Hara et al., 2003 [36]	Case-Control	Age 20-70 Mixed gender Japan	Cruciferous vegetables (cabbage, Japanese white radish, komatsuna, broccoli, Chinese cabbage)	FFQ	All Colorectal cancers	230	115	Median 163 vs 38 grams per 1000kcal	0.64 (0.25-1.63)	Smoking status, alcohol intake, family history of CRC, total energy intake	6

Supplementary Table 1 Descriptive characteristics of included case-control studies (continued)

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of controls	Number of cases	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
Ganesh et al., 2009 [37]	Case-Control	Age 30-75 Mixed gender India	Cruciferous vegetables (cabbage)	Questionnaires	All Colorectal cancers	1628 868 males (53%) 760 females (47%)	203 144 males (71%) 59 females (29%)	consumers vs non-consumers	0.5 (0.30-0.80)	Age, place of residence, religion, occupation, habits (chewing, smoking, alcohol (only males)	6
			Cruciferous vegetables (sprouts)						0.5 (0.40-2.40)		
Inoue et al., 1995 [38]	Case-Control	Males Japan	Cruciferous vegetables (cabbage)	Questionnaires	Proximal colon cancer	8621	257	Consumers vs non-consumers	0.7 (0.4-1.3)	Age	6
					Distal colon cancer				1.1 (0.7-1.8)		
					Rectal cancer				1.2 (0.8-1.7)		
		Females Japan			Proximal colon cancer	23161	175		0.9 (0.5-1.6)		
					Distal colon cancer				1.2 (0.7-2.0)		
					Rectal cancer				1.1 (0.7-1.7)		
Zaridze et al., 1992 [39]	Case-Control	Mixed gender Russia	Cruciferous vegetables (cabbage)	FFQ	All Colorectal cancers	217	217	Highest vs lowest quartile	1.04 (0.53-2.01)	Energy intake, education	6
Bosetti et al., 2012 [41]	Case-Control	Mixed gender Italy	Cruciferous vegetables (cabbage, cauliflower, broccoli, brussels, sprouts, turnip greens)	FFQ Interviews	All Colorectal cancers	11492	2390	>1 vs <1 portion per week	0.83 (0.74-0.94)	Sex, age, study center, year of interview, education, BMI, alcohol, tobacco smoking, total energy intake	7

Supplementary Table 1 Descriptive characteristics of included case-control studies (continued)

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of controls	Number of cases	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
West et al., 1989 [45]	Case-Control	Age 40-79 Males USA	Cruciferous vegetables	FFQ	Colon cancer	391	112	Highest vs lowest quartile	0.3 (0.1-0.8)	Age, BMI, crude fibre, energy intake	7
		Age 40-79 Females USA					119		0.9 (0.4-1.8)		
Freedman et al., 1996 [46]	Case-Control	Mixed gender USA	Cruciferous vegetables (broccoli, brussels sprouts, cabbage, cauliflower, kale, mustard greens)	Questionnaires	All Colorectal cancers	326	163 91 males (58%) 72 females (44%)	Highest vs lowest quartile	0.59 (0.34-1.02)	Age, sex	6
Vogtmann et al., 2014 [47]	Case-Control	Age 40-74 Males China	Cruciferous vegetables (chinese greens, green cabbage, chinese cabbage, bok choy, cabbage, cauliflower, white turnips)	FFQ	All Colorectal cancers	673	340	>122.2 vx <66.8 grams per day	1.06 (0.76-1.50)	Age, BMI, leisure time physical activity, total energy intake, redm eat intake, education, income, occupation, smoking, alcohol consumption, family history of cancer	6

Supplementary Table 2 Descriptive characteristics of included cohort studies

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of participants at baseline	Number of CRC cases	Person years	Length of follow-up (years)	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
Flood et al., 2002 [51]	Cohort	Females (Breast Cancer Detection Demonstration Project) USA	Tomatoes	FFQ Interviews	All Colorectal cancers	45490	485	386142	IQR 8.4 - 9	median of 0.195 vs <0.001 cups per day	0.98 (0.74-1.3)	Multivitamin supplement use, BMI, height, NSAID use, smoking status, education level, physical activity, intake of fruit/grains/red meat/calcium/vitamin D/alcohol.	7
			Cruciferous vegetables (broccoli)							median of 0.08 vs <0.001 cups per day	1.03 (0.78-1.37)		
			Cruciferous vegetables (coleslaw, cabbage, sauerkraut)							median of 0.055 vs <0.001 cups per day	1.11 (0.82-1.49)		
			Cruciferous vegetables (spinach)							median of 0.038 vs <0.001 cups per day	0.93 (0.72-1.21)		
Park et al., 2007 [54]	Cohort	Males Age 50-71 USA	Tomatoes	FFQ	All Colorectal cancers	292094	2048	2121664	4.3	Highest vs lowest quintile	0.94 (0.81-1.21)	Education, physical activity, smoking, alcohol consumption, dietary calcium, total energy	7
			Cruciferous vegetables (broccoli, cauliflower, brussel sprouts)							0.345 vs 0.004 cups per 1000kcal per day	0.93 (0.81-1.07)		
		Females age 50-71 USA	Tomatoes			196949	924			Highest vs lowest quintile	1.01 (0.82-1.24)		
			Cruciferous vegetables (broccoli, cauliflower, brussel sprouts)							0.405 vs 0.045 cup per 1000kcal per day	1.04 (0.84-1.29)		

[a] odds ratio
[b] relative risk
[c] 95% confidence interval
[d] Newcastle-Ottawa Scale

Supplementary Table 2 Descriptive characteristics of included cohort studies (continued)

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of participants at baseline	Number of CRC cases	Person years	Length of follow-up (years)	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
			Citrus fruits							>2 servings per day vs <1 serving per week	1.05 (0.8-1.39)		
			Cruciferous vegetables (cabbage, cauliflower, broccoli, brussels sprouts, coleslaw, kale, sauerkraut)		Colon cancer		937 368 males (39%) 569 females (61%)			>5 servings per week vs <1 serving per day	0.89 (0.68-1.12)		
			Citrus fruits							>2 servings per day vs <1 serving per week	0.97 (0.58-1.64)		
Michels et al., 2000 [50]	Cohort	Mixed gender (nurses aged 30-55, free of cancer, health professionals, dentists, vets, pharmacists, optometrists, osteopaths, podiatrists, aged 40-75) USA	Cruciferous vegetables (cabbage, cauliflower, broccoli, brussels sprouts, coleslaw, kale, sauerkraut)	FFQ	Rectal cancer	136089 47325 males (35 %) 88764 females (65%)	244 89 males (36%) 155 females (64%)	1743645	16	>5 servings per week vs <1 serving per day	0.89 (0.68-1.15)	Age, family history of CRC, prior sigmoidoscopy, height, BMI, physical activity, regular aspirin use, pack years of smoking, vitamin supplement use, alcohol consumption, total caloric intake, red meat consumption, menopausal status, post-menopausal hormone use	7
			Citrus fruits								0.85 (0.7-1.04)		
		Age 45-75 Males Hawaii & California	Cruciferous vegetables			85903	1138				0.87 (0.7-1.08)		
			Citrus fruits								1.04 (0.83-1.13)		
Nomura et al., 2008 [53]	Cohort	Age 45-75 Females Hawaii & California	Cruciferous vegetables	FFQ	All Colorectal cancers	105108	972	>1400000	7.3	Highest vs lowest quintile	0.91 (0.73-1.14)	Ethnicity, age, family history of CRC, history of colorectal polyp, pack-years of cigarette smoking, BMI, hours of vigorous activity, aspirin use, multivitamin use, replacement hormone use (women), log energy intake, alcohol, red meat, folate, vitamin D, calcium	8

Supplementary Table 2 Descriptive characteristics of included cohort studies (continued)

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of participants at baseline	Number of CRC cases	Person years	Length of follow-up (years)	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
Lin et al., 2005 [55]	Cohort	Age >45 Females (mainly nurses, some Hispanics, some other healthcare professionals) USA	Citrus fruits	FFQ	All Colorectal cancers	36976	223	-	10	Median 1.6 vs 0.1 servings per day	1.11 (0.7-1.74)	Age, randomized treatment assessment, BMI, family history of CRC in first degree relatives, history of colon polyps, physical activity, smoking status, baseline aspirin, red meat intake, alcohol consumption, total energy intake, menopausal status, baseline post-menopausal hormone replacement therapy use, folate intake and multivitamin use	6
			Cruciferous vegetables							Median 1.1 vs 0.1 servings per day	0.89 (0.57-1.31)		
McCullough et al., 2003 [56]	Cohort	Age 50-74 Males (cancer prevention study II, Nutrition cohort) USA	Citrus fruits	FFQ	Colon cancer	62609	298	-	-	≥4.6 vs <0.2 servings per day	0.85 (0.58-1.26)	Age, exercise metabolic equivalent (METs), aspirin, smoking, family history of CRC, BMI, education, multivitamin, total calcium, red meat consumption	8
			Cruciferous vegetables (broccoli, mustard greens, turnip greens, collards, coleslaw, cabbage, sauerkraut)							≥0.41 vs <0.8 servings per day	0.74 (0.51-1.08)		
		Age 50-74 Females (cancer prevention study II, Nutrition cohort) USA	Citrus fruits			70554	210			≥4.65 vs <0.2 servings per day	0.71 (0.47-1.07)		
			Cruciferous vegetables (broccoli, mustard greens, turnip greens, collards, coleslaw, cabbage, sauerkraut)							≥0.5 vs <0.11 servings per day	0.91 (0.58-1.44)		

Supplementary Table 2 Descriptive characteristics of included cohort studies (continued)

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of participants at baseline	Number of CRC cases	Person years	Length of follow-up (years)	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
		Age 55-69 Males				1630				167 vs 0 grams per day	1.09 (0.75-1.59)		
		Age 55-69 Females			Colon cancer	1716				187 vs 8 grams per day	1.0 (0.66-1.52)		
		Age 55-69 Males				1630				167 vs 0 grams per day	0.77 (0.49-1.20)		
		Age 55-69 Females	Citrus fruits		Rectal cancer	1716				187 vs 8 grams per day	1.16 (0.63-2.12)		
		Age 55-69 Males				1630					0.76 (0.5-1.13)		
Voorrips et al., 2000 [52]	Cohort	Age 55-69 Females	Cruciferous vegetables (brussels sprouts, cauliflower, cabbage, kale, sauerkraut)	FFQ	All Colorectal cancers	1716	659	-	6.3	58 vs 11 grams per day	0.51 (0.33-0.80)	Alcohol intake, Age, family hisotryr of CRC, other fruits/vegetables	8
			Garlic			41837				>1 vs 0 servings per week	0.68 (0.46-1.02)		
Steinmetz et al., 1994 [58]	Cohort	Age 55-69 Post-menopausal females USA	Cruciferous vegetables (broccoli, cabbage, cauliflower, brussels sprouts)	FFQ	Colon cancer	3521	212	167447	5	>4 vs <1.5 servings per week	1.12 (0.74-1.7)	Age, energy intake	7
					Colon cancer						1.36 (0.79-2.35)		
Dorant et al., 1996 [65]	Cohort	Mixed gender Netherlands	Garlic	FFQ	Rectal cancer	3346 1630 males (49%) 1716 females (51%)	399	978	3.3	Consumption vs no consumption	1.28 (0.63-2.60)	Age, vitamin C & b-carotene, gender, smoking status, education, family history of intestinal cancer, previous history of chronic intestinal disease, cholecystectomy	7
			Garlic							>1 vs 0 servings per week	1.2 (0.8-1.9)		
Sellers et al., 1998 [60]	Cohort	Age 55-69 Females USA	Cruciferous vegetables	FFQ	Colon cancer	35216	241	-	10	>3.5 vs <1.5 servings per week	1.1 (0.8-1.6)	Age, total energy intake, history of rectal colon polyps	8

Supplementary Table 2 Descriptive characteristics of included cohort studies (continued)

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of participants at baseline	Number of CRC cases	Person years	Length of follow-up (years)	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
Giovanucci et al., 1994 [66]	Cohort	Age 40-75 Healthcare professionals Males USA	Garlic	FFQ	Colon cancer	47949	-	-	6	≥2 vs 0 servings per week	0.77 (0.51-1.16)	Age, total energy, previous polyps, previous endoscopic screening, parental history of CRC, total pack years of cigarette smoking, aspirin use, intake of red meat, methionine and alcohol	7
Yang et al., 2016 [71]	Cohort	Age 30-55 Nurses Females USA	Nuts	FFQ	All Colorectal cancers	75680	1503	2103037	30	>5.6 vs 0 grams per day	0.87 (0.72-1.05)	Age, physical activity, family history of CRC, history of previous lower endoscopy, history of UC, history of polyps, aspirin use, multivitamin use, smoking, alcohol intake, total energy intake, BMI, Diabetes mellitus, postmenopausal hormone use, red meat, fruits, vegetables, dietary fibre, , calcium, vitamin D, Mediterranean diet score	7
Yang et al., 2010 [59]	Cohort	Age 40-70 Females Shanghai	Cruciferous vegetables (Chinese greens, green cabbage, Chinese cabbage, cauliflower, white turnip,/radish)	FFQ Interviews	All Colorectal cancers	1573	322	-	-	Highest vs lowest tertial	0.93 (0.66-1.31)	Age, education, household income, physical activity, cigarette smoking, alcohol consumption, BMI, family history of CRC, intake of total energy, fruit, non-cruciferous vegetables, red meat, calcium	7
Singh & Fraser, 1998 [49]	Cohort	Age >25, non hispanic white seventh-day Adventists, mixed gender	Nuts	FFQ	All Colorectal cancers	32051	145	178544	6	>4 vs 0-1 portions per week	0.68 (0.47-1.04	Age, sex, BMI, physical activity, parental history of colon cancer, current smoking, past smoking, alcohol consumption, aspirin use	7
			Cruciferous vegetables				114			>1 portion per day vs 0-2 portions per week	0.74 (0.45-1.19)		

Supplementary Table 2 Descriptive characteristics of included cohort studies (continued)

Author, year	Study design	Population (age, sex, country, specific details on patient demographics)	Dietary exposure	Dietary assessment instrument	Outcomes	Number of participants at baseline	Number of CRC cases	Person years	Length of follow-up (years)	Comparison	OR[a] or RR[b] (95% CI)[c]	Adjusted variables	NOS[d]
Yeh et al., 2006 [73]	Cohort	Males Taiwan	Nuts (peanuts and peanut products)	FFQ	All Colorectal cancers	12026	67	-	10	≥2 vs 0-1 portions per week	0.73 (0.44-1.21)	Aocio-demographic factors, cigarette & alcohol use, BMI, cholesterol, triglyceride, diet, menopause for women)	9
		Females Taiwan				11917	38				0.42 (0.21-0.84)		
Pietinen et al., 1999 [57]	Cohort	Male smokers (>5 cigarettes per day) Alpha-tocopherol, beta carotene Cancer prevention study (ATBC) Males Finland	Cruciferous vegetables	FFQ	All Colorectal cancers	27111	185	-	8	Median 39 vs 0 grams per day	1.6 (1.0-2.3)	Age, smoking years, BMI, alcohol, education, physical activity at work, calcium intake	8

Supplementary Table 3 Number of studies reporting sex and sub-site specific data for each food item

Food item	Study design	Total number of studies	Number of studies reporting only sex-specific results	Number of studies with only non-sex-specific result	Number of studies reporting both sex and non-sex specific results	Number of studies reporting only CRC sub-site specific data (colon or rectum)	Number of studies reporting only non-CRC sub-site specific data (colon and rectum combined)	Number of studies reporting both CRC sub-site specific data (colon or rectum) and combined data
Cruciferous vegetables	All	33	19	13	1	9	24	0
	Case control	21	9 (1 male only)	11	1	4 (2 colon only, 1 rectum only)	17	0
	Cohort	12	10 (4 female only, 1 male only)	2	0	5	7	0
Citrus fruits	All	12	5	5	2	3	8	1
	Case control	7	1	5	1	2	2	1
	Cohort	5	4 (1 female only)	0	1	2 (1 colon only)	2	1
Garlic	All	10	4	6	0	6	4	0
	Case control	6	1	5	0	2 (1 rectum only)	4	0
	Cohort	4	3 (2 female only, 1 male only)	1	0	4 (3 colon only)	0	0
Tomatoes	All	11	4	7	0	2	9	0
	Case control	9	2	7	0	2 (1 rectum only)	7	0
	Cohort	2	2 (1 female only)	0	0	0	2	0
Nuts	All	7	3	4	0	0	7	0
	Case control	4	1	3	0	0	4	0
	Cohort	3	2 (females only)	1	0	0	3	0

Supplementary Table 4 Sensitivity analysis

	Number of studies excluded based on NOS[a]	Pooled OR of all included studies before exclusion based on NOS[a]	Pooled OR of all studies after exclusion of studies with NOS[a] ≤5
Cruciferous vegetables	3	0.90 (0.84-0.95)	0.9 (0.85-0.95)
Citrus fruits	0	-	0.9 (0.84-0.96)
Garlic	2	0.78 (0.69-0.88)	0.83 (0.76-0.91)
Tomatoes	1	0.90 (0.85-0.96)	0.89 (0.84-0.95)
Nuts	0	-	0.72 (0.50-1.03)

[a]Newcastle-Ottawa Scale

Supplementary Table 5 List of food items and predicted anticarcinogenic food compounds used for pathway enrichment analyses[1]

Food category	**Number of compounds**	**Compounds**
Tomato	5	Quercetin, Progesterone, Ferulic acid 4-glucoside, Prolycopene, Lupeol
Cruciferous vegetables	9	Erucin, 1H-Indole-3-methanol, Quercetin, Carvone, Gibberellin A116, Di-2-propenyl sulfide, Brassinin, 4-Methoxyglucobrassicin, Brassinolide
Garlic	5	Quercetin, Di-2-propenyl sulfide, Ajoene, Phloroglucinol, Apigenin
Citrus fruits	10	Umbelliprenin, Luteolin 7-rhamnosylglucoside, Quercetin, Carvone, Obacunone, Quercetagetin, Didymin, Xylan, Tetramethylquercetin, Brassinolide
Nuts	8	Procyanidin B3, Gallic acid, Quercetin, Plumbagin, Betulinic acid, Procyanidin B2, Dihydroxystearic acid, Aesculetin

[1]Obtained from Veselkov et at. [17]

Supplementary Table 6 Top genes and pathways perturbed by food item

Dietary component (active compounds)	**Top 20 genes that interact with active compounds in given food item**	**Top 20 pathways that are overrepresented / affected by given genes according to BIOCARTA database**	**Pathways that are overrepresented / affected by given genes according to PANTHER database**
CITRUS FRUITS Umbelliprenin Luteolin 7-rhamnosylglucoside Quercetin Carvone Obacunone Quercetagetin Didymin Xylan Tetramethylquercetin Brassinolide	CASP3 TP53 PTGS2 UBA52 CASP8 RPS27A CASP9 MAPK8 UBC UBB OAS1 OAS2 BCL2 OAS3 ABCG2 OASL AKT1 POTEF GNB1 GNGT1	1. PPARA 2. IL2RB 3. HIVNEF 4. NFAT 5. MET 6. KERATINOCYTE 7. MAPK 8. RAS 9. INTEGRIN 10. RACCYCD 11. TFF 12. IL2 13. GLEEVEC 14. G1 15. BIOPEPTIDES 16. PDGF 17. EGF 18. IGF1 19. FCER1 20. TCR	5HT Angiogenesis Angiotensin II Apoptosis B cell activation B adrenergic CCKR Corticotropin Dopamine EGF Endogenous cannabinoid signaling Endothelin Enkephalin FAS FGF GABA Gonadotropin Heterotrimeric Histamine Hypoxia Inflammation Insulin/IGF Integrin Interferon Interleukin Etabotropic Nicotine Opioid Oxidative stress response Octocin P53 PDGF PI3 kinase RAS T cell activation TGF beta Thyrotropin Toll receptor VEGF Wnt
CRUCIFEROUS VEGETABLES Erucin 1H-Indole-3-methanol Quercetin Carvone Gibberelline A116 Di-2-propenyl sulfide Brassinin 4-Methoxyglucobrassicin Brassinolide	STAT3 TP53 AKT1 UBA52 SARS2 SARS HYOU1 MAPK1 RPS27A UBC MAPK3 UBB POTEF GNB1 GNGT1 PRKACA NQO1 KCNAB2 GNG13 GNG7	1. NFAT 2. PPARA 3. IL2RB 4. PACCYCD 5. TFF 6. KERATINOCYTE 7. ERK 8. MET 9. BIOPEPTIDES 10. G1 11. HER2 12. INTEGRIN 13. IGF1 14. RAS 15. PDGF 16. AGR 17. MAPK 18. CREB 19. IL2 20. EGF	5HT Alpha adrenergic Angiogenesis Angiotensin II Apoptosis B cell activation B adrenergic CCKR Corticotropin Dopamine EGF Endothelin Enkephalin FAS GR GABA Gonadotrophin Heterotrimeric Histamine Hypoxia Inflammation Insulin/IGF Integrin Interleukin JAK/STAT Metabotropic Muscarinic Nicotine Opioid Oxytocin P 38 MAPK P53 PDGF PI3 kinase RAS T cell activation TGFbeta Thyrotropin Toll receptor VEGF Wnt

Results are shown in order of most to least perturbed for all columns except for '*panther – pathways'* column which are all similarly affected. '*Functional classification'* shows the functions the genes are part of. '*Statistical overrepresentation test'* shows the pathways the genes are preferentially from. BIOCARTA and Panther represent result from different databases.

Supplementary Table 6 Top genes and pathways perturbed by food item (continued)

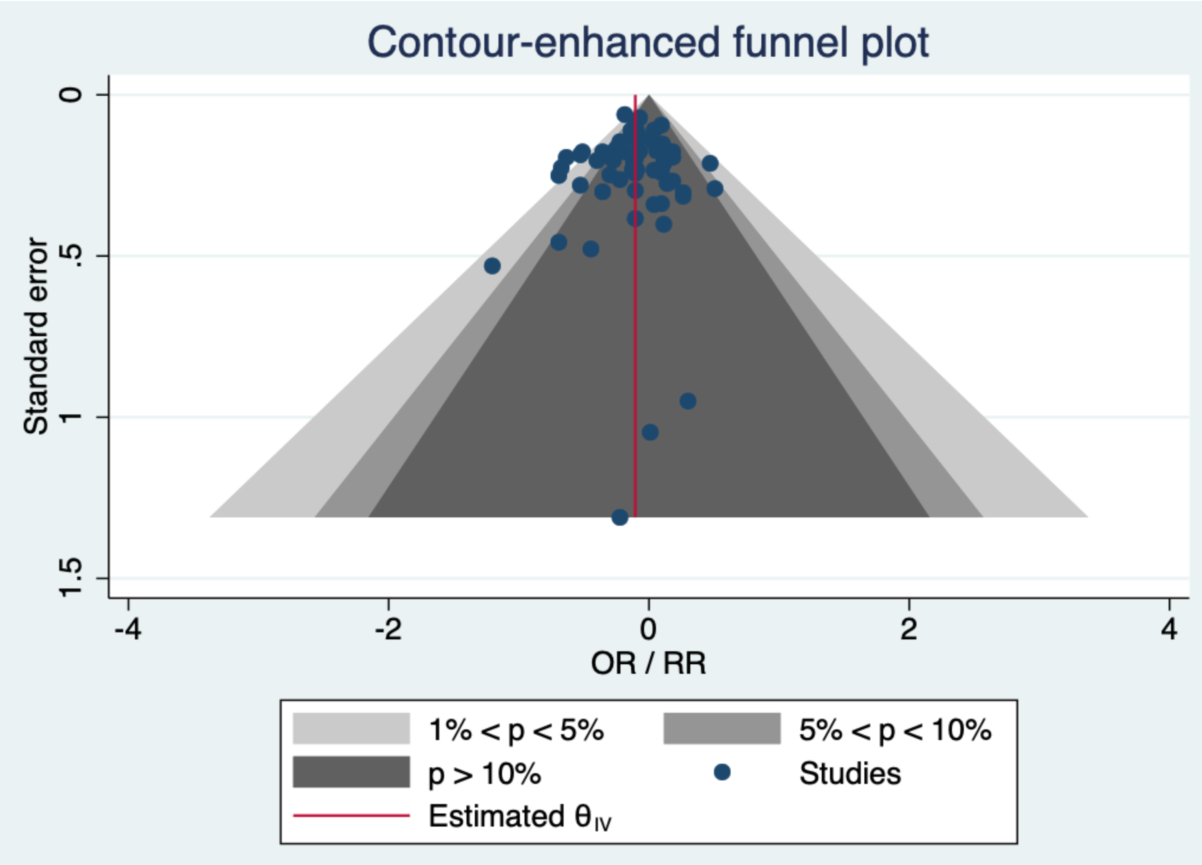
Dietary component (active compounds)	Top 20 genes that interact with active compounds in given food item	Top 20 pathways that are overrepresented / affected by given genes according to BIOCARTA database	Pathways that are overrepresented / affected by given genes according to PANTHER database
GARLIC Quercetin Di-2-propenyl sulfide Ajoene Phloroglucinol Apigenin	TMEM212, AKT1 TP53, IDDM2|INS PTGS2, TFDP1 UBA52, EGLN1 TSPAN19, MAPK1 RPS27A, TFDP2 UBC, EGLN3 UBB, EGLN2 ACLY, SRC FAM123B, PIK3CA	1. RACCYCD 2. PPARA 3. NFAT 4. IL2RB 5. RAS 6. TFF 7. MAPK 8. MET 9. BIOPEPTIDES 10. NGF 11. G1 12. AGR 13. KERATINOCYTE 14. GLEEVEC 15. IL2 16. EGF 17. AKT 18. HER2 19. P53HYPOXIA 20. HIVNEF	Angiogenesis Angiotensin II Apoptosis Axon B cell activation CCKR Cadherin EGF Endothelin FAS FGF Gonadotrophin releasing hormone Hypoxia Inflammation Insulin/IGF Integrin Interferon Interleukin P53 PDGF PI3 kinase Pyruvate RAS T cell activation TGF beta Toll receptor VEGF Wnt
TOMATOES Quercetin Progesterone Ferulic acid 4-glucoside Prolycopene Lupeol	UBA52, CTNNB1 RPS27A, GNGT1 UBC, IDDM2|INS UBB, PRKACA ACACA, SUMO2 ACACB, HSP90AA1 SUMO1, PSMA7 AKT1, PIK3CA GNB1, SUMO3 ACLY	1. IL2RB 2. PPARA 3. NFAT 4. TFF 5. HER2 6. MET 7. KERATINOCYTE 8. TCR 9. EGF 10. MAPK 11. GH 12. BIOPEPTIDES 13. INTEGRIN 14. ERK 15. GLEEVEC 16. G1 17. IGF1 18. RAS 19. INSULIN RACCYCD	5HT Angiogenesis Angiotensin II Apoptosis B cell activation Beta adrenergic CCKR Coricotropin Dopamin EGF Endogenous Endothelin Enkephalin FAS FGF GABA Gonadotrophin-releasing hormone Heterotrimeric Histamine Hypoxia Inflammation Insulin/IGF Integrin Interferon Interleukin Metabotropic Muscarinic Nicotine Opioid Oxidative P53 PDGF PI3 kinase RAS T cell activation TFG beta Thyrotropin Toll receptor VEGF Wnt

Results are shown in order of most to least perturbed for all columns except for '*panther – pathways'* column which are all similarly affected. '*Functional classification'* shows the functions the genes are part of. '*Statistical overrepresentation test'* shows the pathways the genes are preferentially from. BIOCARTA and Panther represent result from different databases.

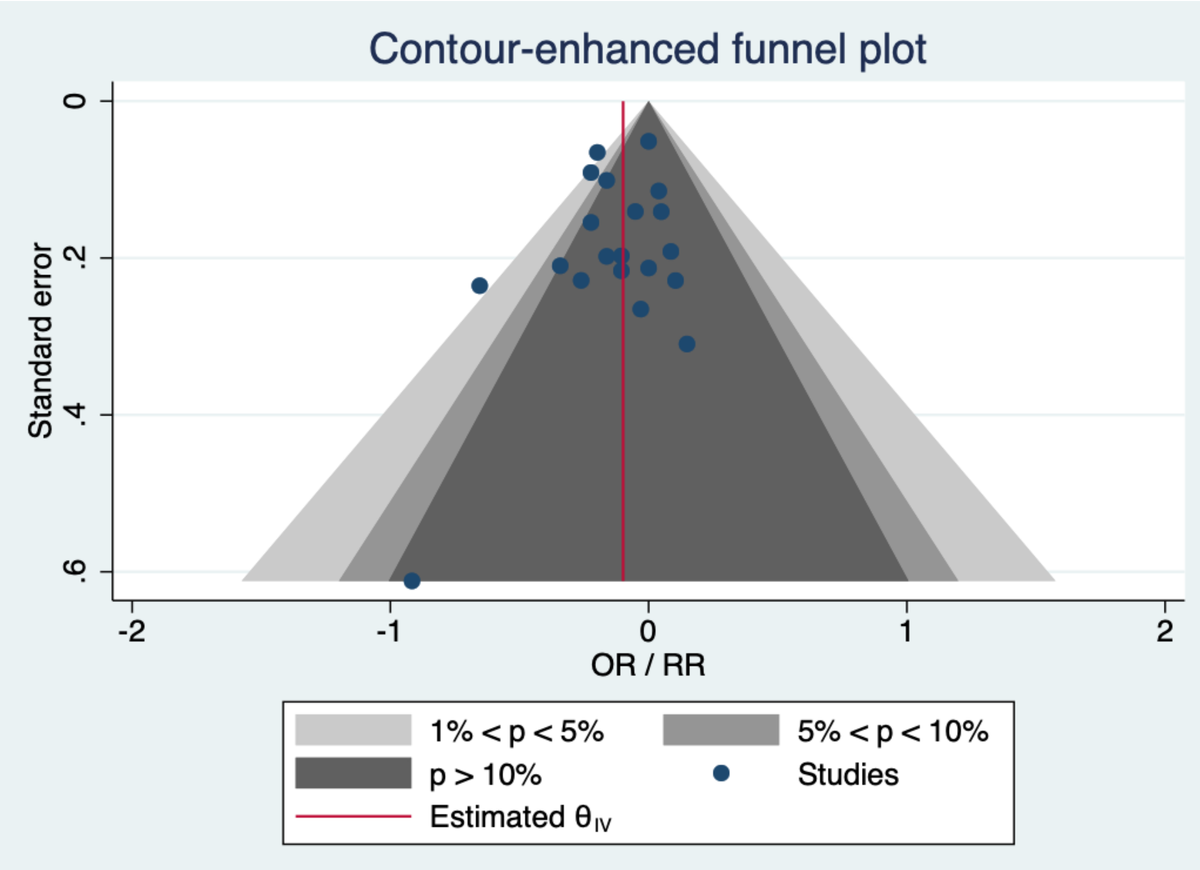
Supplementary Table 6 Top genes and pathways perturbed by food item (continued)

Dietary component (active compounds)	**Top 20 genes that interact with active compounds in given food item**		**Top 20 pathways that are overrepresented / affected by given genes according to BIOCARTA database**		**Pathways that are overrepresented / affected by given genes according to PANTHER database**		
NUTS Procyanidin B3 Gallic Acid Quercetin Plumbagin Betulinic acid Procynidin B2 Dihydroxystearic acid Aesculetin	AKT1 MAPK1 MAPK3 EGFR TP53 TOP2A UBA52 RPS27A NCOA1 UBC	ACACA ACACB UBB CASP9 METTL5 CYP19A1 GAK SLC38A11 PLA2G1B ACLY	1. NFAT 2. TFF 3. PPARA 4. AGR 5. IL2RB 6. KERATINOCYTE 7. RACCYCD 8. MET 9. HER2 10. RAS	11. MAPK 12. INTEGRIN 13. CREB 14. BIOPEPTIDES 15. GH 16. G1 17. GLEEVEC 18. TCR 19. HIVNEF 20. IGF1R	Androgen/ Estrogen/ Progesteron biosynthesis Angiogenesis Angiotensin II Apoptosis B cell activation CCKR Cadherin DNA replication	EGF Endothelin FAS FGF Gonadotrophin releasing hormone Hypoxia Inflammation Insulin/IGF Integrin Interferon Interleukin	P38 MAPK P53 PDGF PI3 kinase Pyruvate Ras T cell activation TFGb Toll receptor VEGF Wnt

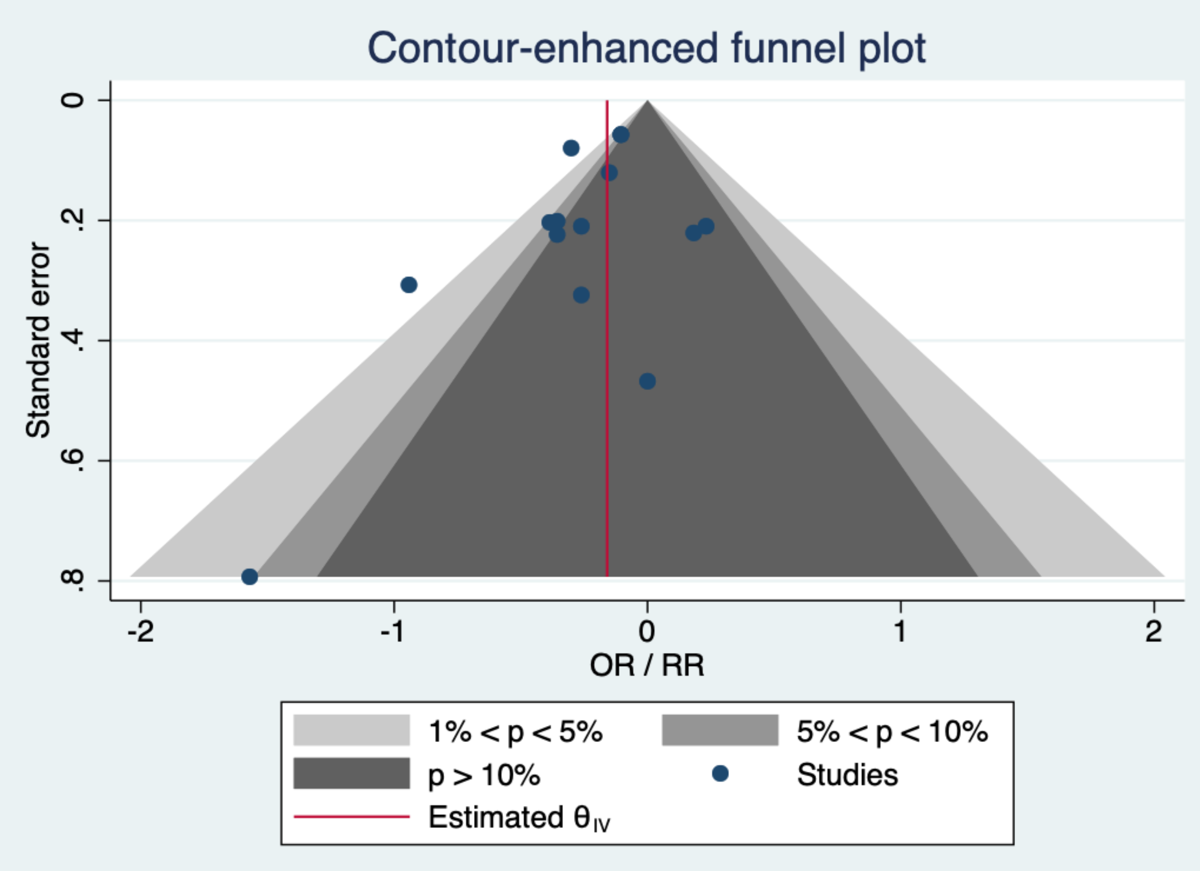
Results are shown in order of most to least perturbed for all columns except for '*panther – pathways'* column which are all similarly affected. '*Functional classification'* shows the functions the genes are part of. '*Statistical overrepresentation test'* shows the pathways the genes are preferentially from. BIOCARTA and Panther represent result from different database.



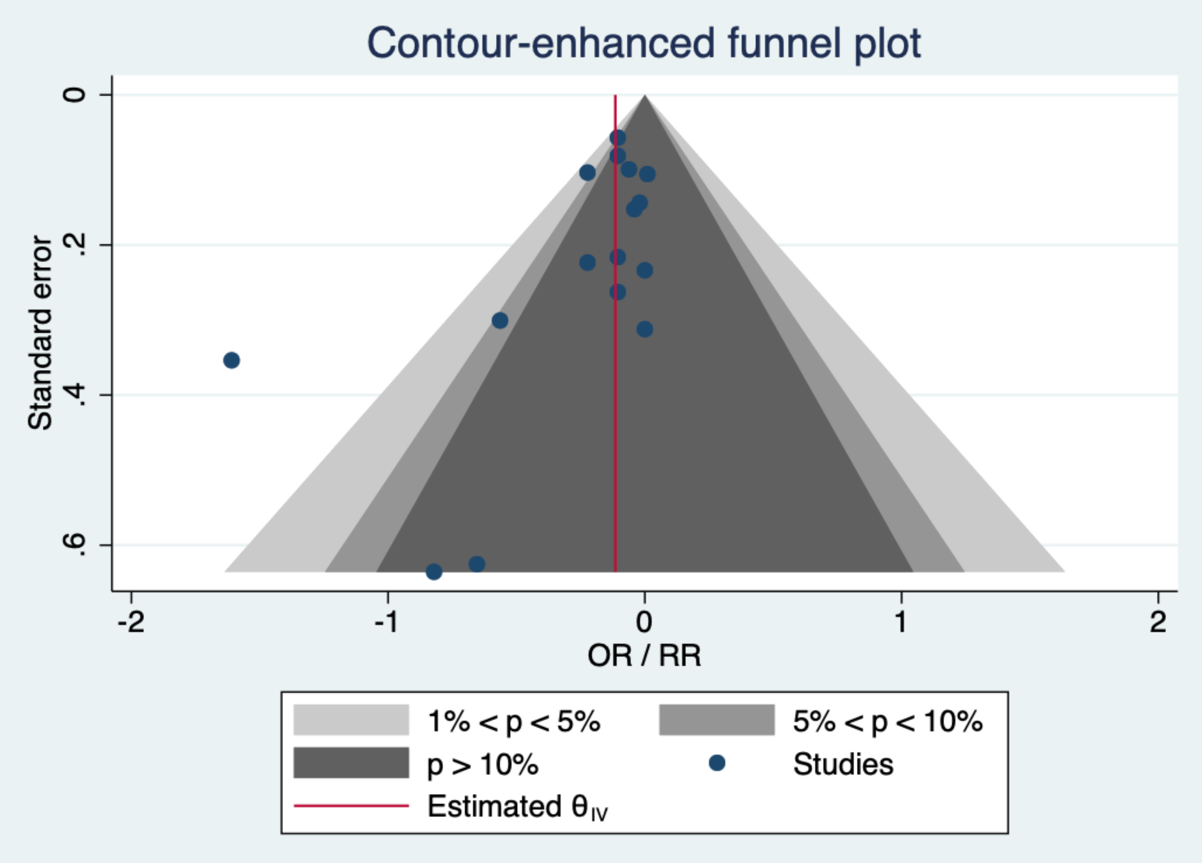
Supplementary Figure 1 Funnel plot of association between cruciferous vegetable intake and colorectal cancer incidence. Scatterplot of the study-specific effect sizes (x axis) versus measures of study precision (y axis). The vertical line represents the estimated overall size effect. Contour lines correspond to varying significance levels of tests of zero effect sizes. Publication bias is suspect if there are studies (especially smaller studies) that are missing in the non-significant regions.



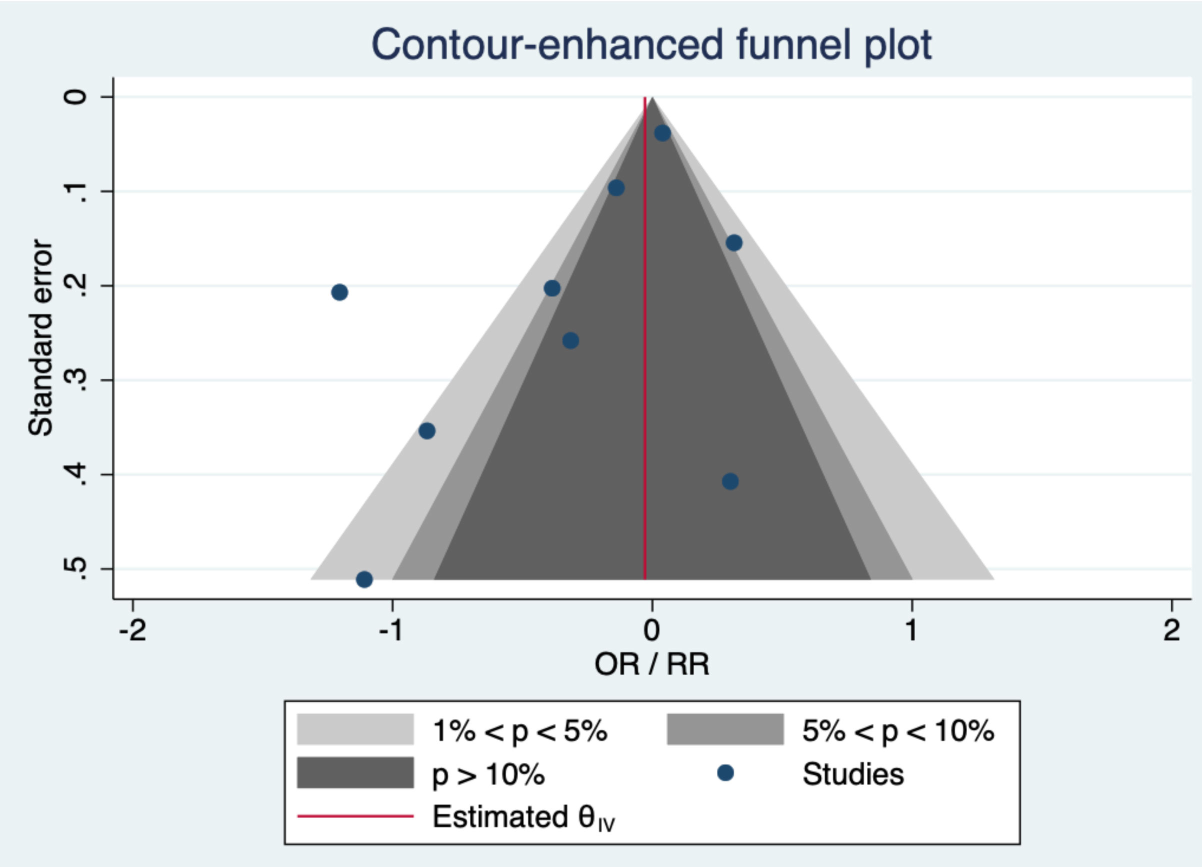
Supplementary Figure 2 Funnel plot of association between citrus fruit intake and colorectal cancer incidence. Scatterplot of the study-specific effect sizes (x axis) versus measures of study precision (y axis). The vertical line represents the estimated overall size effect. Contour lines correspond to varying significance levels of tests of zero effect sizes. Publication bias is suspect if there are studies (especially smaller studies) that are missing in the non-significant regions.



Supplementary Figure 3 Funnel plot of association between garlic intake and colorectal cancer incidence. Scatterplot of the study-specific effect sizes (x axis) versus measures of study precision (y axis). The vertical line represents the estimated overall size effect. Contour lines correspond to varying significance levels of tests of zero effect sizes. Publication bias is suspect if there are studies (especially smaller studies) that are missing in the non-significant regions.



Supplementary Figure 4 Funnel plot of association between tomato intake and colorectal cancer incidence. Scatterplot of the study-specific effect sizes (x axis) versus measures of study precision (y axis). The vertical line represents the estimated overall size effect. Contour lines correspond to varying significance levels of tests of zero effect sizes. Publication bias is suspect if there are studies (especially smaller studies) that are missing in the non-significant regions.



Supplementary Figure 5 Funnel plot of association between nut intake and colorectal cancer. Scatterplot of the study-specific effect sizes (x axis) versus measures of study precision (y axis). The vertical line represents the estimated overall size effect. Contour lines correspond to varying significance levels of tests of zero effect sizes. Publication bias is suspect if there are studies (especially smaller studies) that are missing in the non-significant regions.