



Nutrition and gastrointestinal cancer: An update of the epidemiological evidence



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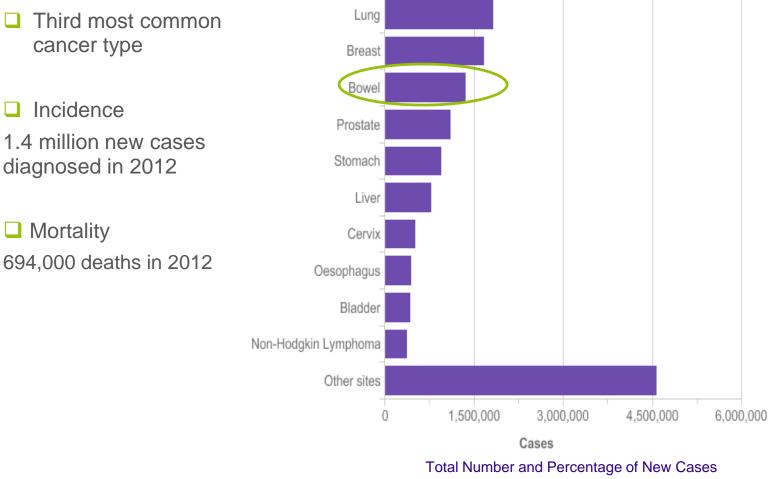
NuGO



28-31 August, 2017

NuGOweek 2017 Varna, Bulgaria

Epidemiology of colorectal cancer

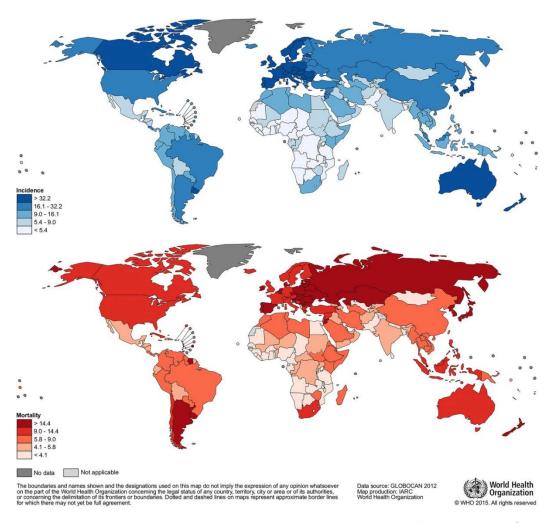


Diagnosed per Year, Worldwide

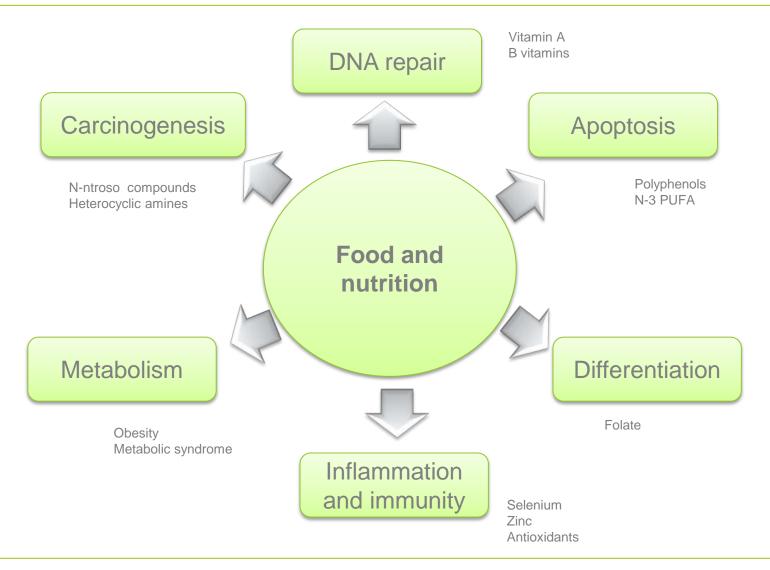
Ferlay et al. Int J Can 2014

Epidemiology of colorectal cancer

- □ 54% of colorectal cancer cases occur in developed countries.
- More deaths (52%) in the less developed regions
- □ Increase by 60% by 2030
 - 2.2 million new cases
 - 1.1 million deaths



Nutrition and cancer promoting mechanisms



To review the meta-epidemiological evidence on the role of nutrition (including body composition) in colorectal cancer in order to identify potential targets for nutritional chemoprevention.







Methods

- Umbrella review of evidence
- An online literature search
 - MEDLINE, ISI Web of Science and Scopus
- Studies published in English (up to June 2017)
- Inclusion criteria:
 - Systematic literature reviews (SLRs) and meta-analyses (MAs) of observational studies
 - Most updated reviews and meta-analyses

Nutrition and colorectal cancer

World Cancer Research Fund American Institute for Cancer Research

Continuous Update Project Keeping the science current



Colorectal Cancer 2011 Report

Food, Nutrition, Physical Activity, and the Prevention of Colorectal Cancer



FOOD, NUTRITION, PHYSICAL ACTIVITY AND CANCERS OF THE COLON AND THE RECTUM 2011

	DECREASES RISK	INCREASES RISK
Convincing	Physical activity ^{1,2} Foods containing dietary fibre ³	Red meat ^{4,5} Processed meat ^{4,6} Alcoholic drinks (men) ⁷ Body fatness Abdominal fatness Adult attained height ⁸
Probable	Garlic Milk ⁹ Calcium ¹⁰	Alcoholic drinks (women) ⁷
Substantial effect on risk unlikely	None identified	

- 1 Physical activity of all types: occupational, household, transport and recreational.
- 2 The Panel judges that the evidence for colon cancer is convincing. No conclusion was drawn for rectal cancer.
- **3** Includes both foods naturally containing the constituent and foods which have the constituent added. Dietary fibre is contained in plant foods.
- 4 Although red and processed meats contain iron, the general category of 'foods containing iron' comprises many other foods, including those of plant origin.
- 5 The term 'red meat' refers to beef, pork, lamb, and goat from domesticated animals.
- 6 The term 'processed meat' refers to meats preserved by smoking, curing, or salting, or addition of chemical preservatives.
- 7 The judgements for men and women are different because there are fewer data for women. For colorectal and colon cancers the effect appears stronger in men than in women.
- 8 Adult attained height is unlikely directly to modify the risk of cancer. It is a marker for genetic, environmental, hormonal, and also nutritional factors affecting growth during the period from preconception to completion of linear growth (see chapter 6.2.13 – Second Expert Report).
- 9 Milk from cows. Most data are from high-income populations, where calcium can be taken to be a marker for milk/dairy consumption. The Panel judges that a higher intake of dietary calcium is one way in which milk could have a protective effect.
- 10 The evidence is derived from studies using supplements at a dose of 1200mg/day.

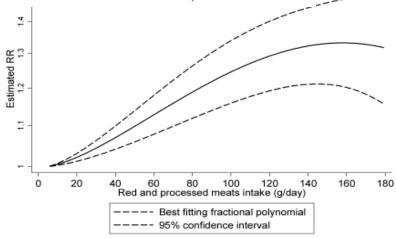
Red and processed meat

Meta-anaylsis

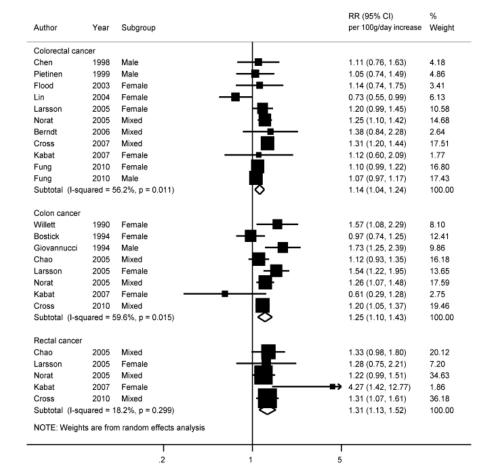
13 prospective studies

Main results

- 14% risk increase in colorectal cancer for every 100 g/day increase of total red and processed meats
 - Non-linear association
 - Above 140 g/day, the risk increase is less pronounced.



Non-linear dose-response meta-analysis



Meta-analyses of red and processed meat consumption and the risk of colorectal cancer

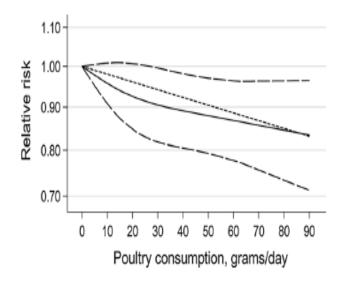
Chan D et al. Plos One 2011

Poultry and colorectal cancer

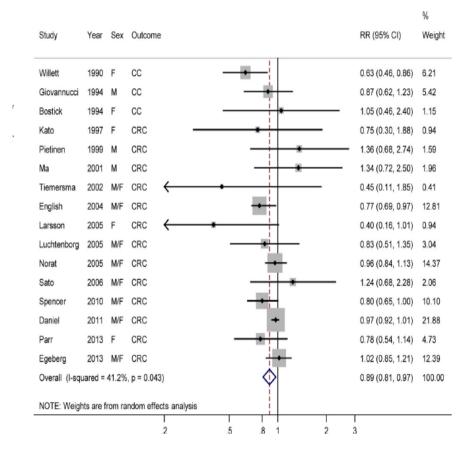
Meta-analysis

- 16 studies

 11% lower risk for the highest versus lowest category of intake



Dose–response analysis between poultry intake and colorectal cancer



Meta-analysis of poultry intake and the risk of colorectal cancer

Shi Y et al. Eur J Nutr 2015

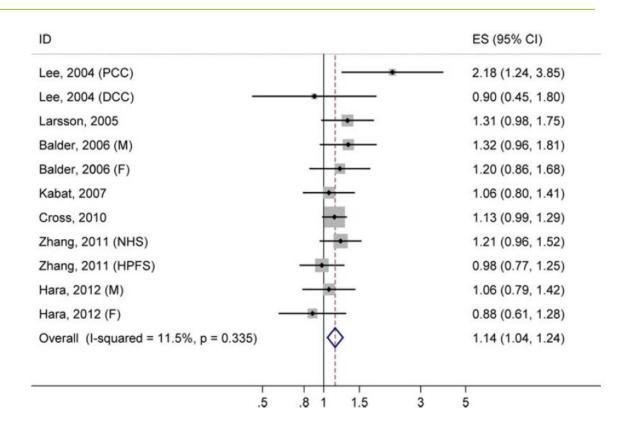
Heme iron

Meta-anaylsis

7 prospective studies

Main results

 14% risk increase in colorectal cancer for high versus low heme iron intake



Meta-analysis of heme iron intake and the risk of colorectal cancer

Qiao& Feng Can Causes Control 2013

Alcohol and colorectal cancer

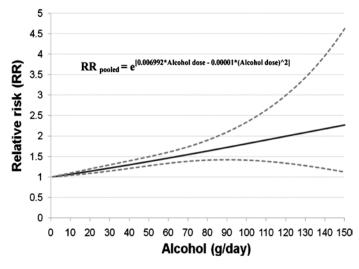
Meta-anaylsis

18 prospective studies

✤ Main results

- 21% higher risk for moderate alcohol drinking
- 52% higher risk for heavy (≥4 drinks/day) alcohol drinking compared to occasional drinking

7%, 38% and 82% higher risk for 10, 50, and 100 g/day of alcohol, respectively

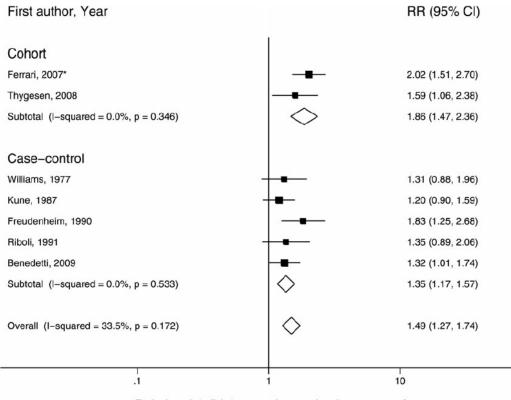


Dose-response meta-analysis of alcohol consumption

Author, year Sex Site Case-control studies Peters, 1989 M CR Longnecker, 1990 M C R Choi, 1991 M C R Biboli, 1991 M C R Barra, 1992 MW C R Peters, 1992 MW C R Barra, 1992 MW C R Boutron, 1995 M C R Murata, 1996 M C R Murata, 1996 M C R Ji, 2002 M C R Sharpe, 2002 M C R All case-control studies (I-squared = 8 Cohort studies Otani, 2003 M Vakai, 2005 M C R	Exp 45 51 64 95 469 116 31 9 269 97 209 111 33.4%, p =	45 57 212 156 979 76 45 12 567 71 176 32 = 0.0001)	NExp 61 168 30 8 354 224 16 34 395 50 503 106	NExp 63 281 105 16 576 236 31 98 1059 77 462 59					RR (95% CI) 0.89 (0.52, 1.51 1.63 (1.05, 2.53 3.53 (2.58, 4.82 1.22 (0.32, 4.59 1.01 (0.83, 1.23 1.67 (1.13, 2.47 1.30 (0.59, 2.86 - 2.16 (0.84, 5.59 0.95 (0.76, 1.18 1.96 (1.20, 3.20 1.17 (0.91, 1.50 2.05 (1.28, 3.30
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Pedersen, 2003 MW C R									
	90	71194	65	74123		- -			1.70 (1.20, 2.40
Wakai, 2005 M C R	69	2821	124	5712			+		1.18 (0.87, 1.60
	97	47460	54	33018		-	-		1.56 (1.11, 2.19
Akhter, 2007 M CR	138	75969	36	34553			+ •	-	1.91 (1.32, 2.77
Ferrari, 2007 MW CR	101	81939	224	409104					1.66 (1.27, 2.16
Lim & Park, 2008 MW CR	10	4291	74	48414					1.11 (0.40, 3.06
Thygesen, 2008 M CR	59	28425	67	71855		- 1			1.75 (1.21, 2.53
All cohort studies (I-squared = 0.0%, j	p = 0.468	3)					\Diamond		1.57 (1.38, 1.80
							1		
All studies (I-squared = 76.4%, p = 0.1	000)						\Leftrightarrow		1.52 (1.27, 1.81
							Ī		

Meta-analysis of alcohol consumption (heavy versus occasional drinkers) and the risk of colorectal cancer

Lifetime alcohol



Relative risk (highest vs lowest intake category)

Meta-analysis of alcohol consumption measured during lifetime/over time and colorectal cancer

Jayasekara et al. Alcohol and Alcoholism 2016

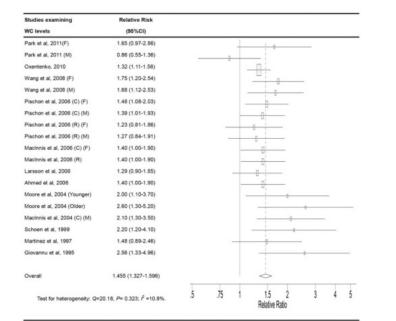
Obesity and colorectal cancer

Meta-anaylsis

- 41 studies on general obesity
- 13 studies on central obesity

Main results

- 33% higher risk for the obese vs. normal category of BMI
- 45% for the highest vs. lowest category of WC



Meta-analysis of general abdominal obesity (waist circumference) and the risk of colorectal cancer

Studies examining	Relative Risk	
BMI levels	(95%CI)	
Park et al. 2011 (F)	1.57 (0.91-2.73)	
Park et al, 2011 (M)	1.06 (0.67-1.69)	
Odegaard et al, 2011	1.25 (1.01-1.55)	
Matsuo et al. 2011 (F)	1.30 (1.00-1.68)	
Matsuo et al, 2011 (M)	1.50 (1.15-1.96)	
watsublet al, 2011 (W)		
Levi et al. 2011 (C)	1.69 (1.24-2.29)	
Levi et al, 2011 (R)	0.86 (0.54-1.34)	
Hughes et al, 2011 (F)	0.97 (0.76-1.24)	I
Hughes et al, 2011 (M)	1.25 (0.96-1.62)	
Oxentenko et al, 2010	1.29 (1.10-1.51)	
Bassett et al. 2010 (F)	1.00 (0.70-1.44)	
Bassett et al, 2010 (M)	1.51 (1.00-2.28)	
Wang et al. 2008 (F)	1.62 (1.04-2.54)	
Wang et al, 2008 (M)	1.76 (1.12-2.76)	
Thygesen et al, 2008	2.29 (1.23-4.26)	
Wang et al, 2007	1.19 (0.97-1.45)	
Reeves et al, 2007	1.01 (0.94-1.09)	+
Lundqvist et al, 2007 (C) (Older)	1.30 (0.90-1.80)	
Lundqvist et al, 2007 (C) (Younger)	1.10 (0.50-2.50)	
Lundqvist et al, 2007 (R) (Older)	0.70 (0.40-1.20)	
Lundqvist et al, 2007 (R) (Younger)	0.90 (0.30-2.50)	
Driver et al, 2007	1.62 (1.09-2.42)	
Adams et al. 2007 (F)	1.28 (0.88-1.85)	
Adams et al, 2007 (M)	2.05 (1.45-2.91)	
Samanic et al, 2007 (M)	1.74 (1.48-2.04)	
Samanic et al, 2006 (R)	1.36 (1.13-1.66)	
Pischon et al, 2006 (C) (F)	1.07 (0.82-1.38)	
Pischon et al, 2006 (R) (F)	1.06 (0.71-1.58)	
Pischon et al, 2006 (C) (M)	1.41 (1.06-1.88)	
Pischon et al, 2006 (R) (M)	1.05 (0.72-1.55)	
MacInnis et al, 2006 (C) (F)	1.00 (0.70-1.40)	
MacInnis et al, 2006 (R) (F)	1.10 (0.70-1.90)	
MacInnis et al, 2006 (R) (M)	1.30 (0.80-2.40)	
Lukanova et al, 2006 (F)	2.01 (1.22-3.27)	
Lukanova et al. 2006 (M)	1.61 (0.95-2.65)	
	1.61 (0.95-2.65)	
Larsson et al, 2006	1.54 (1.08-2.21)	
Bowers et al, 2006	1.66 (1.27-2.18)	
Ahmed et al, 2006	1.54 (0.90-2.80)	
Rapp et al, 2005 (C) (F)	0.88 (0.43-1.81)	
Rapp et al, 2005 (R)(F)	0.96 (0.38-2.39)	
Rapp et al, 2005 (C)(M)	2.48 (1.15-5.39)	
Rapp et al, 2005 (R)(M)	1.66 (1.01-2.73)	
Otani et al, 2005 (C) (F)	0.50 (0.20-1.40)	
Otani et al, 2005 (R) (F)	1.30 (0.50-3.10)	
Otani et al, 2005 (C) (M)	1.40 (0.70-2.80)	
Otani et al, 2005 (R) (M)	1.60 (0.60-3.90)	
Oh et al, 2005 (C)	1.92 (1.15-3.22)	
Oh et al, 2005 (R)	1.08 (0.56-2.10)	
Kuriyama et al, 2005 (F)	2.06 (1.03-4.13)	
Kuriyama et al, 2005 (M)	1.78 (0.73-4.38)	
Engeland et al, 2005 (F)	1.06 (1.02-1.10)	
Engeland et al, 2005 (M)	1.40 (1.32-1.48)	- +
Wei et al, 2004 (C)	1.39 (1.14-1.69)	
Wei et al, 2004 (R)	1.40 (0.96-2.03)	
Moore et al, 2004 (Younger)	1.50 (0.92-2.50)	
Moore et al, 2004 (Older)		
Moore et al, 2004 (Older) MacInnis et al, 2004 (C) (M)	2.40 (1.50-3.90) 1.70 (1.10-2.80)	
Lin et al, 2004	1.67 (1.08-2.59)	
Shimizu et al, 2003 (C) (F)	1.22 (0.69-2.15)	
Shimizu et al, 2003 (R) (F)	0.83 (0.35-1.99)	
Shimizu et al, 2003 (C) (M)	2.11 (1.26-3.53)	
Shimizu et al, 2003 (R) (M)	0.83 (0.42-1.64)	
Terry et al. 2002	1.08 (0.82-1.41)	
Terry et al, 2001	1.24 (0.95-1.62)	
Kaaks et al. 2000	2.83 (1.23-6.54)	
Schoen et al, 1999	1.40 (0.80-2.50)	
Ford et al, 1999	2.79 (1.22-6.35)	
Singh et al, 1998	1.33 (0.88-2.06)	
Chyou et al, 1996 (C)	1.38 (1.01-1.90)	
Chyou et al, 1996 (R)	0.63 (0.38-1.04)	
Bostick et al, 1994	1.41 (0.90-2.23)	
Lee et al, 1992	1.52 (1.06-2.17)	
Lee et al, 1992	1.32 (1.06-2.17)	
Overall	1.334 (1.253-1.420)	.25 .5 .75 1 1.5 2 3 4 5
		25 5 75 1 15 2 3 4 5

Meta-analysis of general obesity (body mass index) and the risk of colorectal cancer

Weight gain and colorectal cancer

Meta-anaylsis

18 prospective studies

Main results

 22 % higher risk for high body weight gain (midpoint: 15.2 kg) compared with stable weight

Study	Design	Sex	Site	Hazard ratio	RR	95% CI
All						
Campbell et al. (22)	Case-control study	Μ	CRC	⊨∎	1.63	[1.27; 2.08]
Campbell et al. (22)	Case-control study	W	CRC		1.13	[0.89; 1.43]
Rapp et al. (19)	Cohort study	М	CC		0.89	[0.58; 1.37]
Rapp et al. (19)	Cohort study	М	RC	i	1.29	[0.68; 2.45]
Rapp et al. (19)	Cohort study	W	CC		1.14	[0.82; 1.60]
Thygesen et al. (18)	Cohort study	М	CC		1.86	[1.21; 2.86]
Bassett et al. (17)	Cohort study	М	CC		2.08	[1.21; 3.57]
Bassett et al. (17)	Cohort study	F	CC	#	1.01	[0.60; 1.68]
Campbell et al. (23)	Case-control study	M, W	CRC	⊨ ∎−	1.68	[1.27; 2.22]
Laake et al. (16)	Cohort study	М	CC	- #-	1.15	[0.86; 1.53]
Laake et al. (16)	Cohort study	W	CC	B	1.10	[0.83; 1.47]
Hughes et al. (15)	Cohort study	М	CRC		1.26	[0.92; 1.73]
Hughes et al. (15)	Cohort study	W	CRC		0.90	[0.69; 1.17]
Renehan et al. (14)	Cohort study	М	CC		1.31	[1.18; 1.45]
Renehan et al. (14)	Cohort study	М	RC	⊦∰-	1.16	[0.97; 1.39]
Renehan et al. (14)	Cohort study	W	CC	-	1.06	[0.91; 1.24]
Renehan et al. (14)	Cohort study	W	RC	- # -	1.26	[0.94; 1.68]
Aleksandrova et al. (13)	Cohort study	M, W	CRC	-] ∎-	1.38	[1.14; 1.66]
Han et al. (11)	Cohort study	Μ	CRC		→ 4.50	[0.79; 25.55]
Han et al. (11)	Cohort study	W	CRC	<	➤ 1.81	[0.14; 23.06]
I ² = 46.3%, P for heteroger	neity=0.013			\$	1.24	[1.14; 1.36]
				1.1		

P for non-linearity=0.463

Meta-analysis of weight gain in adult life and the risk of colorectal cancer

Schlesinger S Aleksandrova K et al. Obes Rev 2013

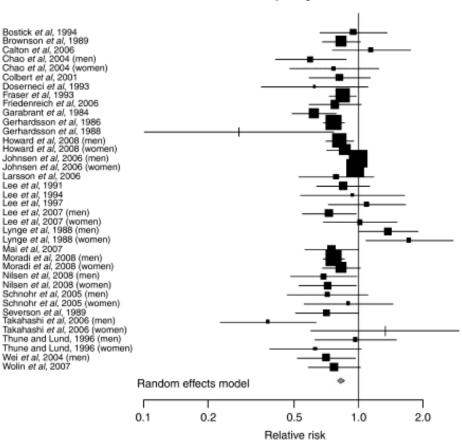
Physical activity and colorectal cancer

Meta-anaylsis

28 cohort

Main results

- 17% lower risk for high vs. low physical activity
- Similar results for men and women



Meta-analysis of physical activity and colon cancer: cohort studies

Wollin K et al. Br J Can 2009

Dietary fibre

Meta-anaylsis

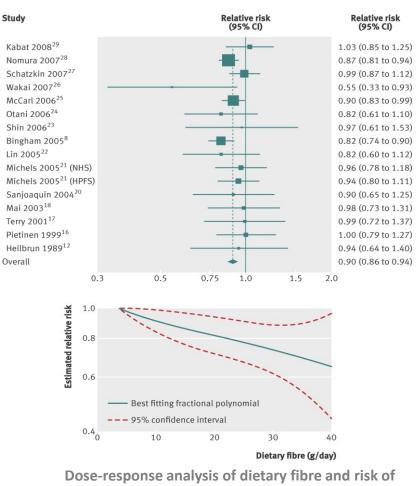
21 prospective studies

Main results

- inverse association between intake of dietary fibre, cereal fibre, and whole grains
- no significant evidence for fibre from fruit, vegetables, or legumes.

Fruit fibre Study	Relative risk (95% CI)	Relative risk (95% CI)	Vegetable fibre Study	Relative risk (95% CI)	Relative risk (95% CI)
Nomura 2007 ³⁸	-	0.88 (0.78 to 0.99)	Nomura 2007 ²⁸		0.93 (0.84 to 1.03)
Schatzkin 200737		1.11 (0.95 to 1.28)	Schatzkin 2007 ²⁷		1.04 (0.89 to 1.21)
Wakai 200726		+ 1.90 (0.40 to 9.04)	Wakai 2007 ³⁶		- 0.71 (0.26 to 1.91)
Bingham 2005 [®]		0.63 (0.33 to 1.19)	Bingham 2005 ⁰		0.78 (0.37 to 1.64)
Lin 2005 ²²		+ 0.90 (0.31 to 2.63)	Lin 2005 ²²		+ 2.32 (0.35 to 15.50
Michels 2005 ²¹ (NHS)		0.76 (0.53 to 1.08)	Michels 2005 ²¹ (NHS)		1.10 (0.81 to 1.51)
Michels 2005 ²¹ (HPFS)		0.83 (0.62 to 1.11)	Michels 2005 ²³ (HPFS)		1.08 (0.83 to 1.41)
Mai 200318		- 1.11 (0.64 to 1.90)	Mai 2003 ¹⁸		0.91 (0.48 to 1.72)
Terry 200117 -		+ 0.97 (0.45 to 2.09)	Terry 200117		+ 3.15 (0.63 to 15.64
Overall	+	0.93 (0.82 to 1.05)	Overall	4	0.98 (0.91 to 1.06)
0.3	0.5 0.75 1.0 1.5	2.0	0.3	0.5 0.75 1.0 1.5	2.0
Legume fibre			Cereal fibre		
Study	Relative risk (95% Cl)	Relative risk (95% CI)	Study	Relative risk (95% CI)	Relative risk (95% Cl)
Schatzkin 200727		0.85 (0.65 to 1.11)	Nomura 2007 ²⁸	-	0.95 (0.84 to 1.07)
			Schatzkin 200727		0.79 (0.67 to 0.93)
Bingham 2005 ⁸		- 1.09 (0.34 to 3.53)	Bingham 20058		0.85 (0.58 to 1.24)
			Lin 2005 ²²		 0.94 (0.28 to 3.12)
Lin 2005 ²²		0.02 (0.00 to 0.37)	Michels 2005 ²³ (NHS)		0.88 (0.63 to 1.24)
Lin 2005 ²²		0.02 (0.00 to 0.37)	Michels 2005 ²³ (NHS) Michels 2005 ²³ (HPFS)	-	
Lin 2005 ⁷²		0.02 (0.00 to 0.37) 0.53 (0.15 to 1.86)		<u> </u>	0.88 (0.63 to 1.24) 0.86 (0.66 to 1.13) 1.01 (0.63 to 1.61)
			Michels 200523 (HPFS)	-	0.86 (0.66 to 1.13)
			Michels 2005 ²³ (HPPS) Mai 2003 ¹⁸		0.86 (0.66 to 1.13) 1.01 (0.63 to 1.61)





colorectal cancer

Aune D et al. BMJ 2011

Fruits and vegetables intake and colorectal cancer risk

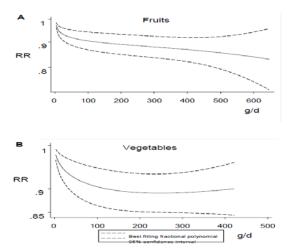
Meta-anaylsis

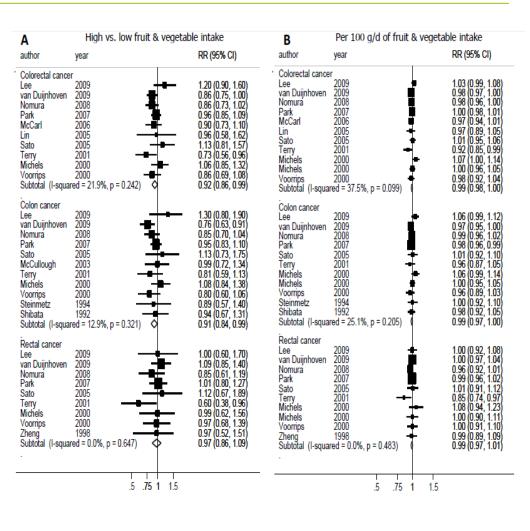
19 prospective cohort studies

Main results

- 8 % lower risk for high vs. low intake
- Non-linear association
- Greatest reduction in risk when increasing intake from very low levels

Figure 5. Fruits and vegetables and colorectal cancer





Dose-response analysis of fruits and vegetables and risk of colorectal cancer

Keum N et al. Int J Can 2014

NuGOweek 2017 Varna, Bulgaria

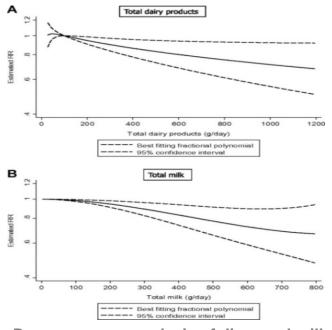
Dairy products

♦Meta-anaylsis

12 cohort studies

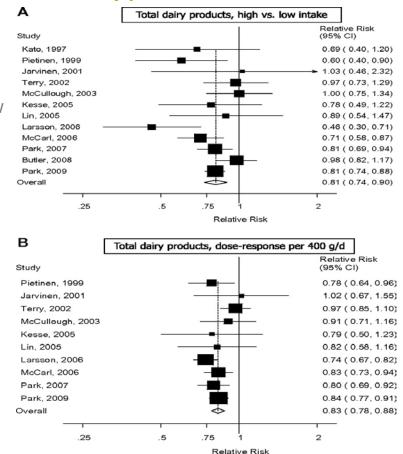
Main results

- 19% lower risk for colon cancer the high versus low intake
- No association for rectal cancer



Dose-response analysis of diary and milk and risk of colorectal cancer

Total dairy products and colorectal cancer



Meta-analysis of dairy products and the risk of colorectal cancer

Aune D. Ann Oncol. 2012

NuGOweek 2017 Varna, Bulgaria

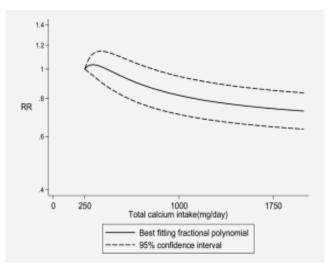
Calcium intake and colorectal cancer risk

Meta-anaylsis

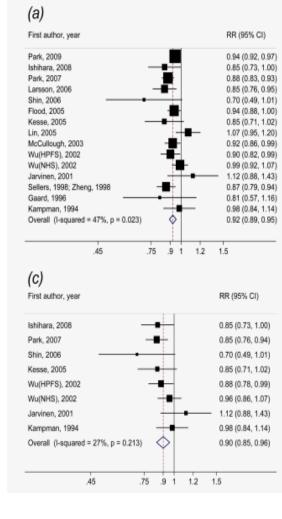
15 prospective cohort studies

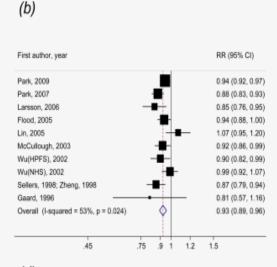
Main results

- Total calcium intake: 8% lower risk for each 300 mg/day increase
- Supplementary calcium: 9% lower risk for each 300 mg/day increase



Dose-response analysis of dietary calcium and risk of colorectal cancer





(d)

		RR (95% CI)
Park, 2009		0.95 (0.92, 0.98)
Park, 2007 -		0.79 (0.69, 0.90)
Flood, 2005	-	0.93 (0.87, 1.00)
Lin, 2005	+	1.11 (0.96, 1.28)
McCullough, 2003		0.86 (0.75, 0.99)
Sellers, 1998		0.85 (0.74, 0.98)
Overall (I-squared = 67%, p = 0.0	09) 🔿	0.91 (0.86, 0.98)

Keum N et al. Int J Can 2014

Vitamin D and colorectal cancer

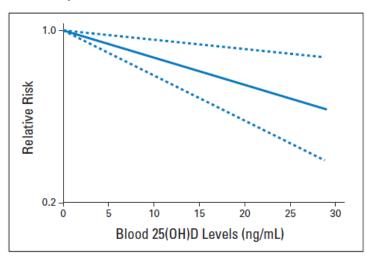
Meta-anaylsis

- 9 prospective cohort studies vitamin D intake
- 9 studies on 25-hydroxyvitamin D [25(OH)D]

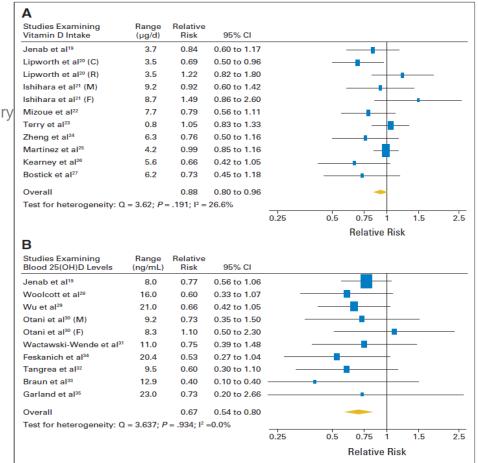
Main results

- 12% lower risk for highest versus lowest category reported vitamin D intake
- 33% lower risk for blood 25(OH)D levels

A 10 ng/mL increment in blood 25(OH)D level conferred an RR of 0.74 (95% CI, 0.63 to 0.89)



Dose-response analysis of blood 25(OH) D levels and risk of colorectal cancer



Relative risks of colorectal cancer for the highest versus lowest categories of (A) vitamin D intake or (B) 25-hydroxyvitamin D [25(OH)D] blood level

Ma Y et al. J Clin Oncol 2011

♦ Meta-anaylsis

 25 prospective cohort studies

✤ Main results

- 8 % lower risk for use versus nonuse of r multivitamins
-14% lower risk for calcium supplements

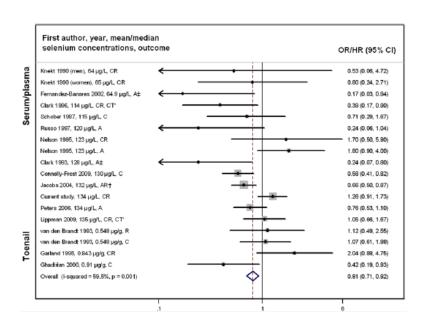
Inconsistent associations: supplemental vitamin A, vitamin C, vitamin E, vitamin D, garlic and folic acid. Summary RRs of "use- no use" meta-analyses and "highest-lowest" metaanalyses for the association of dietary supplement use and colorectal cancer risl

Dietary supplement	Summary RR	95% CI	I ² , p heterogeneity	Included studies	Outcome1
Use-no use meta-analyses					
Multivitamins	0.92	0.87, 0.97	4.9%, <i>p</i> = 0.39	7 ²⁶⁻³²	CRC
Multivitamins (including Pooling Project)	0.92	0.86, 0.98	0.0%, <i>p</i> = 0.43	16 ^{21,28,29,31}	CRC
Vitamin A	0.77	0.62, 0.94	0.0%, <i>p</i> = 0.76	2 ^{3 3,34}	CC
Vitamin C	0.87	0.63, 1.21	77.4%, <i>p</i> = 0.01	3 ³³⁻³⁵	СС
Vitamin E	0.85	0.72, 1.01	20.0%, <i>p</i> = 0.29	5 ³³⁻³⁶	CC
Vitamin D	0.92	0.78, 1.09	53.9%, <i>p</i> = 0.07	5 ^{34,37,38,40,41,}	CRC
Calcium	0.86	0.79, 0.95	63.7%, <i>p</i> = 0.01	834,37,40,42-46	CRC
Garlic	1.24	0.99, 1.54	0.0%, <i>p</i> = 0.34	2 ^{48,49}	CRC
Highest-lowest meta-analyses					
Vitamin A	0.79	0.62, 1.01	0.0%, <i>p</i> = 0.97	2 ^{33,34}	СС
Vitamin C	0.85	0.68, 1.05	10.9%, <i>p</i> = 0.33	3 ³³⁻³⁵	CC
Vitamin E	0.82	0.67, 0.99	11.0%, <i>p</i> = 0.34	5 ³³⁻³⁶	СС
Vitamin D	0.87	0.62, 1.22	67.1%, <i>p</i> = 0.03	4 ^{34,37,39,40}	CRC
Calcium	0.80	0.70, 0.92	49.2%, <i>p</i> = 0.08	6 ^{34,37,40,42-44}	CRC
Folic acid	0.88	0.78, 0.98	6.2%, <i>p</i> = 0.34	3 ^{32,35,47}	CRC

Micronutrients

Selenium

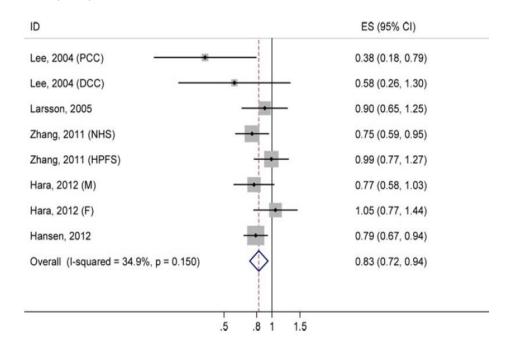
12 observational studies and two clinical trials



Meta-analysis of selenium and the risk of colorectal cancer*

*Ordered by biospecimen type (serum/plasma and toenail samples) and by selenium concentrations within each biospecimen type Takata Y et al. CEBP 2011 Zinc

✤ 6 prospective cohort studies



Meta-analysis of zinc and risk of colorectal cancer

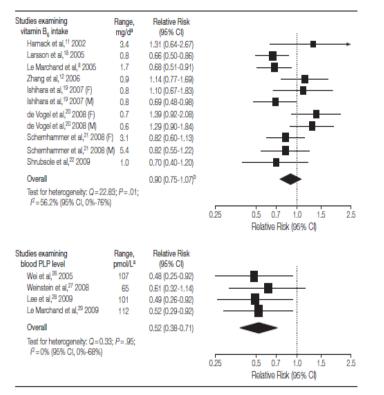
Qiao& Feng Can Causes Control 2013

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One-carbon metabolic pathway

Vitamin B 6

\$9 studies on vitamin B6 intake\$4 studies on blood PLP levels

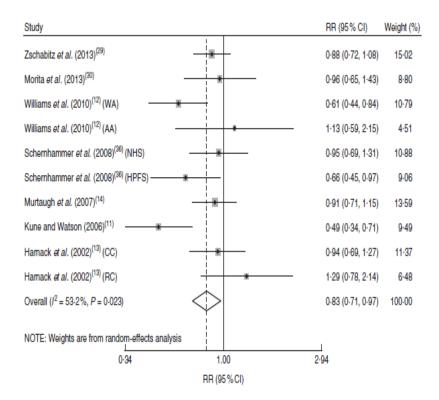


Meta-analysis of vitamin B6 intake or blood PLP Level and risk of colorectal cancer

Larsson S, Orsin N&Yolk A et al. JAMA 2010

Vitamin B 12

17 observational studies (incl 5 cohort studies)



Meta-analysis of vitamin B12 intake and risk of colorectal cancer

Sun NH et al. Public Health Nutrition 2015

NuGOweek 2017 Varna, Bulgaria

Summary

- High body fatness (central adiposity): major risk factor for colorectal cancer
- Other established factors
 - alcohol, red and processed meat intake
 - whole grain intake
- Potential for chemoprevention through optimising micronutrient intakes:
 i.e. calcium, vitamin D, vitamin B6 and B12, zinc and selenium
- However, more data from radomised control trials would be needed

Outlook

Further research focus on

- Complex dietary patterns&lifestyles
- Micronutrients with chemopreventive potential
- Targeted prevention via modulation of cancer-related biomarkers

Prevention focus on

- complex lifestyle recommendations
- patient education about nutritional risks and benefits (i.e. processed meat)
- identification of high-risk individuals
- empowerment for behaviour changes

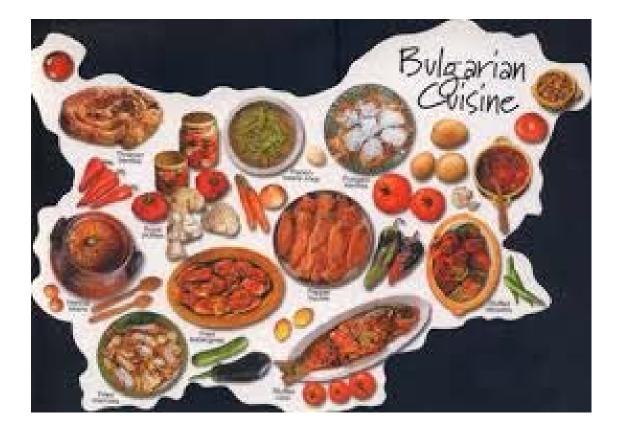
Combined impact of nutritional factors

Lifestyle factor	Index points	Description							
				1.00	•				
Overweight and obesity ^a	0	Overweight or obese: BMI \ge 25 kg/m ² or waist circumference \ge 94 cm for men and \ge 80 cm for women	vals)						D (1 0 0001
	1	Healthy weight: BMI 18 to 25 kg/m 2 or waist circumference <94 for men cm and <80 for women	Inter			•	T		<i>P</i> -trend <0.0001
Physical activity ^b	0	Low and very low physical activity: sedentary or standing occupation and recreational METs \leq 57 for men and METs \leq 82 for women	Confidence Intervals)				+	_	
	1	High and very high physical activity: manual or heavy manual occupation and recreational METs >57 for men and METs >82 for women	-	0.70				Ī	T
Smoking	0	Smoking: current smokers	(95%					•	
	1	Non-smoking: never or former smokers	s (9						•
Alcohol consumption	0	Heavy alcohol consumption: not adherent to alcohol consumption recommendations of WCRF/AICR (2007) [15] for two standard drinks a day (>24 g/day) for men and one standard drink a day (>12 g/day) for women	ard ratios						
1	Limited alcohol consumption: adherent to alcohol consumption recommendations of WCRF/AICR (2007) [15,16] for two standard drinks a day (\leq 24 g/day) for men and one standard drink a day (\leq 12 g/day) for women	Hazard	0.50					1	
Diet quality ^c	0	Unhealthy diet quality: 0 to 4 points of the diet index of colorectal cancer related foods		00	r 1 (Reference)	2	3	4	5
	1	Healthy diet quality: 5 to 8 points of the diet index of colorectal cancer related foods					Number of lifes	tyle factors	

Based on data from 350 000 men and women in the EPIC cohort

Aleksandrova K et al. BMC Medicine 2014

THANK YOU FOR YOUR ATTENTION!



Biomarkers of Obesity

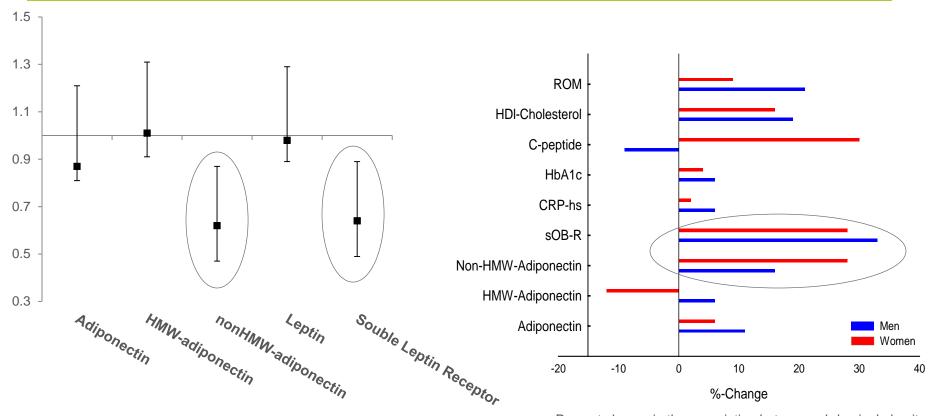
Adipose tissue Mechanism Adiposity Established relationship with Activates insulin resistance IGFR Play a role in the regulation of Varying levels of Tumor Development Cell insulin signaling and action Adipocytokines **IGF-1** Increases Proliferation Source of inflammation Increases Insulin Insulin Increases Apoptosis Resistance Adipocytokines Decreases

- Leptin
- Adiponectin
- IL-6
- TNFalpha
- Free fatty acids
- Resistin

Does obesity drive these changes in hormones or do hormones drive changes in body shape, weight, and adiposity?

Activates IR

Biomarkers of Obesity: Data from the EPIC cohort



Multivariable-adjusted RRs associated with an increase in continuous log-transformed biomarker concentrations.

Models are stratified for EPIC center, age, sex, fasting status, date of blood collection, and adjusted for smoking status, education, alcohol, physical activity, red and processed meat, fish and shellfish ,fruits and vegetables, body mass index and waist circumference.

Percent change in the association between abdominal obesity and colon cancer with adjustment for biomarkers



Analysing research on cancer prevention and survival

Evidence matrix

Convincing decreased risk Probable decreased risk Convincing increased risk Probable increased risk Substantial effect on risk unlikely	MOUTH, PHARYNX, LARYNX (2007)	NASOPHARYNX (2007)	OESOPHAGUS (2016)	LUNG (2007)	STOMACH (2016)	PANCREAS (2012)	GALLBLADDER (2015)	LIVER (2015)	COLORECTUM (2011)	BREAST PREMENOPAUSE (2010)	BREAST POSTMENOPAUSE (2010)	OVARY (2014)	ENDOMETRIUM (2013)	PROSTATE (2014)	KIDNEY (2015)	BLADDER (2015)
Foods containing dietary fibre																
Aflatoxins																
Non-starchy vegetables ¹																
Allium vegetables																
Garlic																
Fruits ²																
Red meat																
Processed meat ³																
Cantonese-style salted fish																
Diets high in calcium ⁴																
Foods preserved by salting																
Glycaemic load																
Arsenic in drinking water																
Mate ^s																
Alcoholic drinks ⁶			_													
Coffee																
Beta-carotene ⁷																
Physical activity [®]																
Body fatness ⁹			_													
Adult attained height ¹⁰																
Greater birth weight																
Lactation																









Whole grains and colorectal cancer

Study

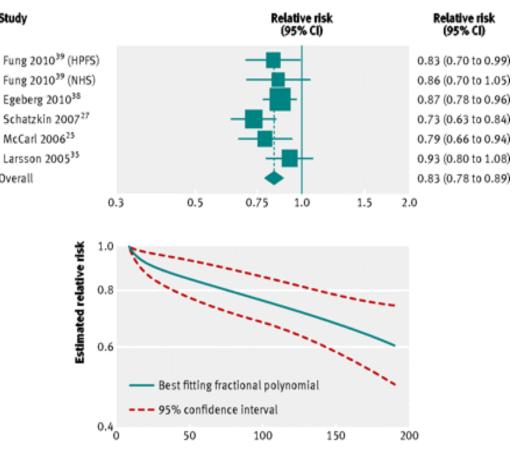
Overall

* **Meta-anaylsis**

6 studies

Main results **

- 10% reduction in risk of colorectal cancer for each 10 g/day intake of total dietary fibre and cereal fibre
- 20% reduction for each three . servings (90 g/day) of whole grain daily



Whole grains (g/day)

Meta-analysis of whole grains and the risk of colorectal cancer