Supplementary Material

A comparison of methods in estimating population attributable risk for colorectal cancer in the United States

Hanseul Kim, Kai Wang, Mingyang Song, Edward L. Giovannucci

Supplementary Table 1. Literature-based method: Distribution of exposures in the National Health and Nutrition Examination Survey (NHANES)

Supplementary Table 2. Literature-based method: Relative risks for the associations between risk factors and colorectal cancer in the United States

Supplementary Table 3. Low-risk method: Characteristics throughout follow-up according to cutoff 7

Supplementary Table 4. Additional analysis: Relative risks from studies other than what we used for the literature-based method

Supplementary Table 5. Additional analysis: Population attributable risk (PAR) for colorectal cancer using US-specific relative risk (RR)

Supplementary Table 6. Additional analysis: Minimum and maximum population attributable risk (PAR) for colorectal cancer in the United States, derived from different sources of prevalence estimates for body fatness and cigarette smoking

Supplementary Table 7. Additional analysis: Distribution of exposures from sources other than what we used for the literature-based method

Supplementary Methods

Supplementary Table 1. Literature-based method: Distribution of exposures in the National Health and Nutrition Examination Survey (NHANES)*

Exposure	Exposure category/unit	Prevalence, %	
		Men	**Women**
Physical activity**	0-249 MET-m/week	54.8	57.9
	250-499 MET-m/week	7.5	9.0
	500-749 MET-m/week	4.9	6.6
	750-999 MET-m/week	5.9	5.4
	≥ 1000 MET-m/week	27.1	21.1
Body fatness/BMI	**Normal (18.5-< 25 kg/m^2)**	22.2	28.7
	Overweight (25-29.9 kg/m^2)	40.9	29.6
	Obese (≥ 30 kg/m^2)	36.3	40.1
Alcohol	**None**	29.4	40.7
	< 1 drink/day	32.0	37.7
	1-< 4 drinks/day	24.4	16.9
	≥ 4 drinks/day	14.4	4.8
Red meat	**0-9 g/day**	1.1	4.8
	10-24 g/day	9.5	30.2
	25-49 g/day	30.3	46.6
	50-74 g/day	29.5	15.6
	75-99 g/day	17.9	2.5
	≥ 100 g/day	11.7	0.3
Processed meat	**0-4 g/day**	0.9	11.7
	5-24 g/day	29.4	60.0
	25-49 g/day	41.6	22.8
	50-74 g/day	19.6	4.4
	≥ 75 g/day	8.5	1.0
Dietary fiber	0-9 g/day	9.1	17.5
	10-19 g/day	53.2	63.3
	20-29 g/day	30.9	17.8
	≥ 30 g/day	6.7	1.4
Dietary calcium	0-199 mg/day	0.0	0.1
	200-399 mg/day	1.3	3.8
	400-599 mg/day	7.8	16.2
	600-799 mg/day	16.9	26.4
	800-999 mg/day	21.3	24.4
	≥ 1000 mg/day	52.6	29.1
Cigarette smoking	**Never**	50.8	63.2
	Former	30.2	21.8
	Current	19.0	15.0

*These were weighted prevalence estimates calculated by Islami et al, 2018[1] for adults ≥30 years. Exposure distribution data on alcohol drinking and cigarette smoking were obtained from the National Health Interview Survey (NHIS). Data on all other exposures were obtained from the NHANES.

**Moderate or vigorous activity.

Supplementary Table 2. Literature-based method: Relative risks for the associations between risk factors and colorectal cancer in the United States

	In original reports				In this analysis when our exposure categories were different from those in original reports		
Exposure	**Exposure category/unit**	**Region; Study design**	**Relative risk (95% CI)**		**Exposure category/unit**	**Relative risk**	
			Men	**Women**		**Men**	**Women**
Physical activity[2]	Higher vs. lower (90th percentile vs. 10th percentile)	US and Europe; Pooled analysis	Colon: 0.84 (0.77, 0.91) Rectum: 0.87 (0.80, 0.95)	Colon: 0.84 (0.77, 0.91) Rectum: 0.87 (0.80, 0.95)	0-249 MET-m/week 250-499 MET-m/week 500-749 MET-m/week 750-999 MET-m/week **≥ 1000 MET-m/week**	1.19 1.14 1.09 1.04 Reference	1.19 1.14 1.09 1.04 Reference
Body fatness/BMI[3]	**Normal (18.5-< 25 kg/m^2)** Overweight (25-29.9 kg/m^2) Obese (≥ 30 kg/m^2)	Worldwide; Meta-analysis	Reference 1.17 (1.12, 1.22) 1.38 (1.32, 1.44)	Reference 1.07 (1.01, 1.14) 1.17 (1.06, 1.30)	Same	Same	Same
Alcohol[4]	**None** Light (0.1-12.5 g/day) Moderate (12.6-50 g/day) Heavy (> 50 g/day)	Worldwide; Meta-analysis	Reference 1.05 (0.95, 1.16) 1.21 (1.11, 1.32) 1.53 (1.30, 1.80)	Reference 0.95 (0.89, 1.01) 1.07 (0.99, 1.16) 1.24 (0.68, 2.25)	**None** < 1 drink/day 1-< 4 drinks/day ≥ 4 drinks/day	Same	Reference 1.00 1.07 1.24
Red meat[5]	Per 100 g/day increase	Worldwide; Report	Colon: 1.22 (1.06, 1.39) Rectum: 1.13 (0.96, 1.34)	Colon: 1.22 (1.06, 1.39) Rectum: 1.13 (0.96, 1.34)	**0-9 g/day** 10-24 g/day 25-49 g/day 50-74 g/day 75-99 g/day ≥ 100 g/day	Reference 1.02 1.06 1.11 1.16 1.21	Reference 1.02 1.06 1.11 1.16 1.21
Processed meat[5]	Per 50 g/day increase	Worldwide; Report	Colon: 1.23 (1.11, 1.35) Rectum: 1.08 (1.00, 1.18)	Colon: 1.23 (1.11, 1.35) Rectum: 1.08 (1.00, 1.18)	**0-4 g/day** 5-24 g/day 25-49 g/day 50-74 g/day ≥ 75 g/day	Reference 1.04 1.13 1.23 1.33	Reference 1.04 1.13 1.23 1.33
Dietary fiber[5]	Per 10 g/day increase	Worldwide; Report	0.89 (0.82, 0.96)	0.91 (0.87, 0.96)	0-9 g/day 10-19 g/day 20-29 g/day **≥ 30 g/day**	1.42 1.26 1.12 Reference	1.33 1.21 1.10 Reference

Dietary calcium[5]	Per 200 mg/day increase	Worldwide; Report	0.93 (0.88, 0.99)	0.93 (0.91, 0.95)	0-199 mg/day 200-399 mg/day 400-599 mg/day 600-799 mg/day 800-999 mg/day **≥ 1000 mg/day**	1.44 1.34 1.24 1.16 1.08 Reference	1.44 1.34 1.24 1.16 1.08 Reference
Cigarette smoking[6]	Never Former Current	US; Meta-analysis	Reference 1.20 (1.10, 1.30) 1.40 (1.20, 1.70)	Reference 1.20 (1.10, 1.30) 1.60 (1.40, 1.90)	Never Former Current	Same	Same

Supplementary Table 3. Low-risk method: Characteristics* throughout follow-up according to cutoff 7

	NHS		HPFS	
	Cutoff <7 (high-risk)	Cutoff ≥7 (low-risk)	Cutoff <7 (high-risk)	Cutoff ≥7 (low-risk)
Person-years (% within cohort)	1,775,750 (95)	96,756 (5)	936,616 (95)	48,843 (5)
Age, years	60.7 (11.6)	65.5 (11.3)	63.9 (11.3)	66.7 (11.5)
White, %	98	98	94	95
Physical activity				
Continuous, min/day	21.0 (17.6)	41.2 (21.2)	28.2 (32.7)	61.8 (42.2)
Moderate-to-vigorous intensity activity for ≥30 minutes/day, %	24	76	34	89
Body mass index				
Continuous, kg/m^2	25.6 (4.6)	22.6 (2.4)	25.9 (3.3)	23.3 (1.9)
≥18.5 and <25 kg/m^2, %	54	92	42	92
Alcohol intake				
Continuous, g/day	6.2 (9.4)	3.2 (4.1)	11.3 (14.0)	5.5 (6.5)
<14 (women) or <28 (men) g/day, %	86	99	88	99.6
Red meat				
Continuous, serving/day	0.6 (0.3)	0.3 (0.2)	0.6 (0.4)	0.2 (0.2)
<0.5 serving/day, %	36	94	47	98
Processed meat				
Continuous, serving/day	0.3 (0.3)	0.1 (0.1)	0.3 (0.3)	0.1 (0.1)
<0.2 serving/day, %	38	97	40	98
Dietary fiber				
Continuous, g/day	16.2 (4.4)	23.2 (4.7)	21.6 (5.9)	32.2 (7.5)
≥20 (women) or ≥30 (men) g/day, %	17	85	7	68
Total calcium intake				
Continuous, mg/day	932.1 (339.9)	1310.2 (338.4)	923.5 (362.0)	1291.4 (408.7)
>1,000 mg/day, %	38	89	32	84
Cigarette smoking				
Pack-years**	23.7 (20.3)	8.8 (12.5)	24.6 (19.0)	11.0 (12.4)
Never smoking or past smoking with pack-years <5, %	54	89	53	92

*Updated information throughout follow-up was used to calculate the means for continuous variables and percentage for categorical variables. All variables are age-standardized except person-years and age.

**Among ever smokers only

Supplementary Table 4. Additional analysis: Relative risks from studies other than what we used for the literature-based method

Exposure	Study; Exposure category/unit	Region; Study design	Relative risk (95% CI)	
			Men	**Women**
Physical activity	Kyu et al, 2016[7]*	Worldwide; Meta-analysis		
	< 600 MET-m/week		Reference	Reference
	600-3999 MET-m/week		0.90 (0.85, 0.95)	0.90 (0.85, 0.95)
	4000-7999 MET-m/week		0.83 (0.77, 0.90)	0.83 (0.77, 0.90)
	≥ 8000 MET-m/week		0.79 (0.74, 0.85)	0.79 (0.74, 0.85)
Body fatness/BMI	Calle et al, 2004[8]	Worldwide; Review		
	Normal (18.5-< 25 kg/m^2)		Reference	Reference
	Overweight (25-29.9 kg/m^2)		1.5	1.2
	Obese (≥ 30 kg/m^2)		2.0	1.5
	Moghaddam et al, 2007[9]	Worldwide; Meta-analysis		
	Normal (18.5-< 25 kg/m^2)		Reference	Reference
	Overweight (25-29.9 kg/m^2)		1.16 (1.07, 1.27)	1.03 (0.96, 1.10)
	Obese (≥ 30 kg/m^2)		1.40 (1.33, 1.47)	1.07 (0.97, 1.18)
Alcohol	Fedirko et al, 2011[10]	Worldwide; Meta-analysis		
	None		Reference	Reference
	Light (0.1-12.5 g/day)		1.02 (0.92, 1.14)	0.95 (0.89, 1.01)
	Moderate (12.6-50 g/day)		1.24 (1.13, 1.37)	1.08 (1.03, 1.13)
	Heavy (> 50 g/day)		1.62 (1.31, 2.01)	1.54 (1.04, 2.29)
Red meat	Zhao et al, 2017[11]	Worldwide; Meta-analysis		
	Per 100 g/day		1.16 (1.05, 1.29)	1.16 (1.05, 1.29)
Processed meat	Zhao et al, 2017[11]	Worldwide; Meta-analysis		
	Per 50 g/day		1.22 (1.12, 1.33)	1.22 (1.12, 1.33)
Dietary fiber	Aune et al, 2011[12]	Worldwide; Meta-analysis		
	Per 10 g/day		0.92 (0.82, 1.03)	0.94 (0.89, 0.99)
Dietary calcium	Keum et al, 2014[13]**	Worldwide; Meta-analysis		
	Per 300 mg/day		0.92 (0.89, 0.95)	0.93 (0.89, 0.96)
Cigarette smoking	Liang et al, 2009[14]	Worldwide; Meta-analysis		
	Never		Reference	Reference
	Former		1.20 (1.04, 1.38)	1.20 (1.04, 1.38)
	Current		1.15 (1.00, 1.32)	1.15 (1.00, 1.32)

*Results on colon cancer

**Results on total calcium intake

Supplementary Table 5. Additional analysis: Population attributable risk (PAR) for colorectal cancer using US-specific relative risk (RR)

Exposure*	Exposure category/unit	Worldwide RR (95% CI)	US-specific RR (95% CI)	Worldwide PAR, %	US PAR, %
Body fatness/BMI[15]	**Normal** Obese (≥ 30 kg/m^2)	Reference 1.33 (1.25, 1.42)	Reference 1.47 (1.33, 1.62)	11	15
Alcoholic drink[4]	**None** Light (≤ 12.5 g/day) Moderate (12.6-50 g/day) Heavy (> 50 g/day)	Reference 0.99 (0.95, 1.04) 1.17 (1.11, 1.24) 1.44 (1.25, 1.65)	Reference 0.96 (0.90, 1.03) 1.14 (1.05, 1.24) 1.29 (1.01, 1.66)	7	4
Red meat[11]	Highest vs. Lowest	1.12 (1.03, 1.21)	1.07 (0.99, 1.16)	1	0
Processed meat[11]	Highest vs. Lowest	1.15 (1.07, 1.24)	1.12 (1.04, 1.21)	1	1
Dietary fiber[12]	Per 10 g/day	0.90 (0.86, 0.94)	0.92 (0.88, 0.96)	18	14
Dietary calcium[13]	Per 300 mg/day**	0.92 (0.89, 0.95)	0.93 (0.90, 0.96)	6	5
				Total Estimate	
				37	***35***

*Exposure categories: Body fatness/BMI (Normal, Obese (≥ 30 kg/m^2)); Alcoholic drink (None, Light (≤ 12.5 g/day), Moderate (12.6-50 g/day), Heavy (> 50 g/day)); Red meat (Highest vs. lowest; 0-9 g/day vs. ≥ 100 g/day); Processed meat (Highest vs. lowest; 0-4 g/day vs. ≥ 75 g/day); Dietary fiber (0-9 g/day, 10-19 g/day, 20-29 g/day, ≥ 30 g/day); Dietary calcium (0-199 mg/day, 200-399 mg/day, 400-599 mg/day, 600-799 mg/day, 800-999 mg/day, ≥ 1000 mg/day)

**Results on total calcium intake

Supplementary Table 6. Additional analysis: Minimum and maximum population attributable risk (PAR) for colorectal cancer in the United States, derived from different sources of prevalence estimates for body fatness and cigarette smoking

Exposure*	**(Minimum PAR, Maximum PAR), %**	
	Men	**Women**
Physical activity	10	11
Body fatness/BMI	(16, 17)	(7, 8)
Alcoholic drinks	13	2
Red meat	9	5
Processed meat	12	6
Dietary fiber	18	17
Dietary calcium	6	10
Cigarette smoking	(12, 16)	(12, 16)
Total estimate	***(64, 67)***	***(53, 56)***

*Exposure categories same as Table 2

Supplementary Table 7. Additional analysis: Distribution of exposures from sources other than what we used for the literature-based method*

Exposure	Source; Exposure category/unit	Prevalence, %	
		Men	Women
Body fatness/BMI	NCD-RisC, 2016		
	Overweight (25-29.9 kg/m^2)	38.1	26.6
	Obese (≥ 30 kg/m^2)	36.5	38.2
	WHO Global InfoBase, 2016		
	Overweight (25-29.9 kg/m^2)	37.2	26.2
	Obese (≥ 30 kg/m^2)	35.5	37.0
	BRFSS, 2018		
	Overweight (25-29.9 kg/m^2)	40.5	29.5
	Obese (≥ 30 kg/m^2)	30.6	31.3
Cigarette smoking	NHANES[16]**		
	Never	27.7	56.6
	Former	47.6	25.8
	Current	24.6	24.2

*Note that prevalence estimates for standard calculations (Supplementary Table 1) were weighted prevalence estimates from NHANES except for alcohol drinking and cigarette smoking that were obtained from the National Health Interview Survey (NHIS). (Islami et al, 2018[1])

**Prevalence estimates were calculated among adults aged 50 to 74. Never-smoker was defined as those having smoked <100 cigarettes in their lifetime.

Supplementary Methods

Assumptions for each of the factors

Physical activity

For the literature-based method, we used relative risk (RR) from a pooled analysis of the US and European studies that examined physical activity[2]. Hazard ratios (HRs) were used to estimate RRs. In their supplementary figure, the authors presented HRs stratified by sex. However, we did not use the stratified values because P for heterogeneity by sex was >0.05 for colon cancer and rectal cancer. As there is ~70% colon cancer and ~30% rectal cancer[17], we took a weighted average of colon cancer and rectal cancer to calculate the RR for CRC: 0.84*0.70 + 0.87*0.30 = 0.849. The non-BMI adjusted HR was 0.849 for 90th versus 10th percentile (i.e., highest vs. lowest category). The median and interquartile range of 6 of the 7 cohorts included was 8 (2-22) MET-hours/week. Therefore, for our physical activity categories (0-249, 250-499, 500-749, 750-999, ≥1000 MET-m/week), we assumed that the HR of 0.849 could be used for the RR comparing ≥1000 MET-m/week category to 0-249 MET-m/week (reference) category.

For each of the categories, we calculated the RRs: 0-249 MET-m/week: 1/0.849; 250-499 MET-m/week: EXP(LN(0.849)/1000*250)/0.849; 500-749 MET-m/week: EXP(LN(0.849)/1000*500)/0.849; 750-999 MET-m/week: EXP(LN(0.849)/1000*750)/0.849; ≥1000 MET-m/week: 1

Body fatness/body mass index (BMI)

According to the WCRF/AICR report[5], there was a significant non-linear dose-response relationship for BMI. We used a meta-analysis of studies for BMI that stratified by sex[3]. There were 12 cohorts from all over the world, and 5 out of 12 cohorts were from the US.

Alcohol intake

According to the WCRF/AICR report[5], there was a significant non-linear dose-response relationship for alcohol intake. We used a dose response meta-analysis of 66 studies from the world and 27 studies were from North America[4].

Red meat and processed meat intakes

We used a dose-response meta-analysis from the WCRF/AICR report for red meat and processed meat intakes[5]. For robustness, we used studies for colon cancer and studies for rectal cancer, separately, not studies that looked at combined CRC. As there is ~70% colon cancer and ~30% rectal cancer[17], we took a weighted average of colon cancer and rectal cancer to calculate the RR for CRC.

For red meat, there was no sex-specific RR reported. We assumed that there is no heterogeneity by sex. There were 11 studies for colon cancer (summary RR = 1.22 per 100 g/day) and 8 studies for rectal cancer (summary RR = 1.13 per 100 g/day). For the RR of CRC, we calculated the weighted average: 1.22*0.70 + 1.13*0.30 = 1.193. For each of the categories, we calculated the RRs: 0-9 g/day: 1; 10-24 g/day: EXP(LN(1.193)/100*12.5); 25-49 g/day: EXP(LN(1.193)/100*32.5); 50-74 g/day: EXP(LN(1.193)/100*57.5); 75-99 g/day: EXP(LN(1.193)/100*82.5); ≥100 g/day: EXP(LN(1.193)/100*107.5)

For processed meat, there was no sex-specific RR reported. We assumed that there is no heterogeneity by sex. There were 12 studies for colon cancer (summary RR = 1.23 per 50 g/day) and 10 studies for rectal cancer (summary RR = 1.08 per 50 g/day). For the RR of CRC, we calculated the weighted average: 1.23*0.70 + 1.08*0.30 = 1.185. For each of the categories, we calculated the RRs: 0-4 g/day: 1; 5-24 g/day: EXP(LN(1.185)/50*12.5); 25-49 g/day: EXP(LN(1.185)/50*35); 50-74 g/day: EXP(LN(1.185)/50*60); ≥75 g/day: EXP(LN(1.185)/50*85)

Fiber intake

We used a dose-response meta-analysis from the WCRF/AICR report for dietary fiber intake[5]. There were 6 studies for men and 11 studies for women.

For each of the categories, we calculated the RRs:

For men: 0-9 g/day: 1/EXP(LN(0.89)/10*30); 10-19 g/day:0.89/EXP(LN(0.89)/10*30); 20-29 g/day: EXP(LN(0.89)/10*20)/EXP(LN(0.89)/10*30); ≥30 g/day: 1

For women: 0-9 g/day: 1/EXP(LN(0.91)/10*30); 10-19 g/day:0.91/EXP(LN(0.91)/10*30); 20-29 g/day: EXP(LN(0.91)/10*20)/EXP(LN(0.91)/10*30); ≥30 g/day: 1

Calcium intake

We used a dose-response meta-analysis from the WCRF/AICR report for dietary calcium intake[5]. There were 3 studies for men and 9 studies for women.

For each of the categories, we calculated the RRs: 0-199 mg/day: 1/EXP(LN(0.93)/200*1000); 200-399 mg/day: 0.93/EXP(LN(0.93)/200*1000); 400-599 mg/day: EXP(LN(0.93)/200*400)/EXP(LN(0.93)/200*1000); 600-799 mg/day: EXP(LN(0.93)/200*600)/EXP(LN(0.93)/200*1000); 800-999 mg/day: EXP(LN(0.93)/200*800)/EXP(LN(0.93)/200*1000); ≥1000 mg/day: 1

Cigarette smoking

We used a meta-analysis of US studies for cigarette smoking[6]. There were 3 cohorts for men and 4 cohorts for women.

Details on the low-risk method

We used the Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS) for the low-risk method, which are two ongoing US cohorts that enrolled 121,700 registered female nurses aged 30 to 55 years in 1976[18] and 51,529 male health professionals aged 40 to 75 years in 1986[19], respectively. In both cohorts, participants completed a detailed questionnaire about their lifestyle and medical information at baseline and every two years thereafter with over 90% of follow-up. This study was approved by the institutional review boards of the Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health, and those of participating registries as required.

Participants also provided dietary information through validated food frequency questionnaires (FFQs) every 4 years. Among participants who returned the baseline questionnaires (1980 for the NHS and 1986 for the HPFS, when we first collected detailed dietary and lifestyle information), we excluded those who had a history of cancer (except nonmelanoma skin cancer), or ulcerative colitis; with a BMI of <18.5 kg/m^2; reported implausible energy intakes (<500 or >3500 kcal/d for women; <800 or >4200 kcal/d for men); or with missing data on lifestyle exposures. After these exclusions, 60,275 women and 41,544 men were included in the analysis.

Height, body weight, cigarette smoking, and physical activity were self-reported through biennial questionnaires. Cigarette smoking was evaluated based on both pack-years and the current status that was reported biennially. Physical activity was assessed by the total hours per week for moderate-to-vigorous intensity activity (including brisk walking) that requires the expenditure of at least 3 metabolic equivalents per hour. Alcohol use and diet were self-reported every 4 years by the FFQs.

In the cohorts, we calculated person-years of follow-up for each participant from the date of returning the baseline questionnaire until the date of CRC diagnosis, death, loss to follow-up, or end of follow-up (June 30, 2014, for the NHS and January 31, 2014, for the HPFS), whichever came first.

To transform servings to grams for red and processed meat, we used the following formula:
Grams of red meat = sum of (Beef, pork or lamb as a sandwich in servings/day)*84.54, (Beef or lamb as a main dish in servings/day)*140, (Pork as a main dish in servings/day)*140.78, (Hamburger, regular in servings/day)*85, and (Hamburger, lean in servings/day)*85
Grams of processed meat= sum of (Bacon in servings/day)*16, (Hot dogs in servings/day)*46.05, (Salami, bologna sandwich in servings/day)*56, (Chicken or turkey hot dogs or sausage in servings/day)*50.72, and (Other Processed meats in servings/day)*54

Details on the additional analyses

In the additional sensitivity analyses for the literature-based method, we sought to explore the impact of the following components in the literature-based method: 1) choice of risk factors, 2) different sources of RR estimates, and 3) different sources of exposure prevalence estimates.

1) To address how inclusion/exclusion of certain risk factors affects the population attributable risk (PAR) estimates, we included only the "convincing" factors (and cigarette smoking) and excluded the factors that have been defined as "probable" by the WCRF/AICR[5] from the calculation of PAR. To be specific, we calculated the proportion of CRC attributable to lifestyle factors excluding red meat, dietary fiber, and dietary

calcium, resulting in these 5 factors: physical activity, body fatness/BMI, alcoholic drinks, processed meat, and cigarette smoking.

2) To find the different sources of RRs, we performed searches in PubMed. Recent meta-analyses (published within 20 years) were the most preferred source of RRs, followed by large pooled analyses (or a review that summarized the literature). RRs had to provide the most relevant information to our study (e.g., sex-specific RRs); studies that reported RRs that matched our predefined exposure category levels were preferred. For each of the risk factors, we calculated PARs with different RRs and provided a range of PAR estimates (minimum PAR, maximum PAR) that could be obtained with more than one source of RR. In addition, we performed a sensitivity analysis with RRs stratified by countries to assess whether using US-specific RRs results in different PAR estimates compared to using worldwide RRs.

3) To assess how different sources of prevalence estimates change the PAR, we evaluated different prevalence estimates for the two factors: body fatness and cigarette smoking. Not enough information was provided on other factors. Prevalence estimates had to be sex-specific and nationally representative. In addition, the sources had to match the defined categories for BMI (normal, overweight, and obese) and cigarette smoking (never, former, and current).

References

1. Islami F, Goding Sauer A, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, McCullough ML, Patel AV, Ma J, Soerjomataram I, Flanders WD, Brawley OW, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. *CA: a cancer journal for clinicians* 2018;**68**: 31-54.

2. Moore SC, Lee IM, Weiderpass E, Campbell PT, Sampson JN, Kitahara CM, Keadle SK, Arem H, Berrington de Gonzalez A, Hartge P, Adami HO, Blair CK, et al. Association of Leisure-Time Physical Activity With Risk of 26 Types of Cancer in 1.44 Million Adults. *JAMA Intern Med* 2016;**176**: 816-25.

3. Xue K, Li FF, Chen YW, Zhou YH, He J. Body mass index and the risk of cancer in women compared with men: a meta-analysis of prospective cohort studies. *European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP)* 2017;**26**: 94-105.

4. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, Scotti L, Jenab M, Turati F, Pasquali E, Pelucchi C, Galeone C, et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *British journal of cancer* 2015;**112**: 580-93.

5. World Cancer Research Fund International/American Institute for Cancer Research, Continuous Update Project Report: Diet, Nutrition, Physical Activity and Colorectal Cancer, 2017.

6. Carter BD, Abnet CC, Feskanich D, Freedman ND, Hartge P, Lewis CE, Ockene JK, Prentice RL, Speizer FE, Thun MJ, Jacobs EJ. Smoking and mortality--beyond established causes. *N Engl J Med* 2015;**372**: 631-40.

7. Kyu HH, Bachman VF, Alexander LT, Mumford JE, Afshin A, Estep K, Veerman JL, Delwiche K, Iannarone ML, Moyer ML, Cercy K, Vos T, et al. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013. *BMJ (Clinical research ed)* 2016;**354**: i3857.

8. Calle EE, Kaaks R. Overweight, obesity and cancer: epidemiological evidence and proposed mechanisms. *Nature reviews Cancer* 2004;**4**: 579-91.

9. Moghaddam AA, Woodward M, Huxley R. Obesity and risk of colorectal cancer: a meta-analysis of 31 studies with 70,000 events. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* 2007;**16**: 2533-47.

10. Fedirko V, Tramacere I, Bagnardi V, Rota M, Scotti L, Islami F, Negri E, Straif K, Romieu I, La Vecchia C, Boffetta P, Jenab M. Alcohol drinking and colorectal cancer risk: an overall and dose-response meta-analysis of published studies. *Annals of oncology : official journal of the European Society for Medical Oncology* 2011;**22**: 1958-72.

11. Zhao Z, Feng Q, Yin Z, Shuang J, Bai B, Yu P, Guo M, Zhao Q. Red and processed meat consumption and colorectal cancer risk: a systematic review and meta-analysis. *Oncotarget* 2017;**8**: 83306-14.

12. Aune D, Chan DS, Lau R, Vieira R, Greenwood DC, Kampman E, Norat T. Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. *BMJ (Clinical research ed)* 2011;**343**: d6617.

13. Keum N, Aune D, Greenwood DC, Ju W, Giovannucci EL. Calcium intake and colorectal cancer risk: dose-response meta-analysis of prospective observational studies. *International journal of cancer* 2014;**135**: 1940-8.

14. Liang PS, Chen TY, Giovannucci E. Cigarette smoking and colorectal cancer incidence and mortality: systematic review and meta-analysis. *International journal of cancer* 2009;**124**: 2406-15.

15. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. *PloS one* 2013;**8**: e53916.

16. Stokes A, Preston SH. How smoking affects the proportion of deaths attributable to obesity: assessing the role of relative risks and weight distributions. *BMJ Open* 2016;**6**: e009232.

17. Siegel RL, Miller KD, Goding Sauer A, Fedewa SA, Butterly LF, Anderson JC, Cercek A, Smith RA, Jemal A. Colorectal cancer statistics, 2020. *CA: a cancer journal for clinicians* 2020.

18. Colditz GA, Manson JE, Hankinson SE. The Nurses' Health Study: 20-year contribution to the understanding of health among women. *J Womens Health* 1997;**6**: 49-62.

19. Rimm EB, Giovannucci EL, Willett WC, Colditz GA, Ascherio A, Rosner B, Stampfer MJ. Prospective study of alcohol consumption and risk of coronary disease in men. *Lancet* 1991;**338**: 464-8.