

## Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1. Baseline characteristics according to BMI in NHSII, 1989**

Characteristics <sup>a</sup>	Baseline BMI (1989)			
	18.5-22.9 kg/m <sup>2</sup>	23-24.9 kg/m <sup>2</sup>	25-29.9 kg/m <sup>2</sup>	≥ 30 kg/m <sup>2</sup>
Age, years	34.4 (4.6)	35.1 (4.7)	35.5 (4.6)	35.9 (4.5)
BMI at age 18, kg/m <sup>2</sup>	19.9 (2.0)	21.4 (2.5)	22.6 (3.0)	25.9 (4.8)
Weight change since age 18, kg	2.8 (5.4)	6.6 (6.8)	12.1 (8.7)	24.8 (14.3)
Height, cm	165 (7)	164 (6)	165 (7)	164 (7)
Postmenopausal, %	2.0	2.3	2.4	3.3
Family history of colorectal cancer, %	4.2	4.1	4.3	4.0
Screening lower endoscopy within past 10 years, %	1.2	1.3	1.3	1.2
Lower endoscopy due to other indications within past 10 years <sup>b</sup> , %	1.7	1.9	1.9	2.5
History of diabetes, %	0.7	0.9	1.4	4.6
Ever smokers, %	34	35	35	34
Pack-years among ever smokers	10.8 (7.9)	11.6 (8.2)	12.0 (8.2)	12.4 (8.6)
Alcohol intake, g/day	4.3 (7.4)	4.0 (7.1)	3.5 (6.9)	2.3 (5.8)
Physical activity, MET-hours/week	26.9 (37.9)	23.8 (34.6)	21.4 (31.4)	17.4 (27.8)
Regular aspirin use, %	11	11	12	13
Regular NSAID use, %	17	19	22	28
Current use of multivitamin, %	47	45	44	41
Total calories, kcal/day	1,771 (538)	1,772 (538)	1,807 (559)	1,851 (576)
Red meat intake, servings/week	5.6 (4.4)	6.1 (4.5)	6.6 (4.8)	7.5 (5.3)
Fiber intake, g/day	18.5 (5.7)	18.4 (5.4)	18.2 (5.2)	17.5 (5.1)
Folate intake, µg/day	490 (296)	478 (291)	464 (282)	437 (271)
Calcium intake, mg/day	1,027 (443)	1,025 (433)	1,019 (432)	984 (425)
Alternate Healthy Eating Index 2010	44.4 (10.5)	44.3 (10.4)	43.8 (10.2)	42.2 (10.4)

Abbreviations: BMI, body mass index; MET, metabolic equivalent of tasks; NSAID, non-steroid anti-inflammatory drugs.

<sup>a</sup> Mean (SD) is presented for continuous variables.

<sup>b</sup> Lower endoscopy due to indications other than for screening (e.g. having symptoms, family history of colorectal cancer, follow-up endoscopy, or positive fecal occult blood test)

**eTable 2. Sensitivity analysis on BMI and risk of early-onset colorectal cancer**

	<b>BMI</b>					
	18.5-22.9 kg/m <sup>2</sup>	23-24.9 kg/m <sup>2</sup>	25-29.9 kg/m <sup>2</sup>	≥ 30 kg/m <sup>2</sup>	Each 5 kg/m <sup>2</sup> increase	<i>P</i> -trend <sup>c</sup>
<b>Cumulative average BMI</b>						
Cases	37	20	36	21		
Person-years	522,309	226,168	273,390	174,585		
Age-adjusted RR (95% CI)	1 [Reference]	1.12 (0.65-1.93)	1.62 (1.02-2.57)	1.44 (0.84-2.46)	1.16 (1.00-1.35)	0.06
Multivariable-adjusted RR (95% CI) <sup>b</sup>	1 [Reference]	1.15 (0.67-1.99)	1.63 (1.02-2.62)	1.50 (0.85-2.64)	1.18 (1.00-1.39)	0.05
<b>BMI with 4-year lag</b>						
Cases	29	14	27	25		
Person-years	374,706	166,090	213,305	155,853		
Age-adjusted RR (95% CI)	1 [Reference]	0.97 (0.51-1.84)	1.41 (0.83-2.40)	1.67 (0.97-2.87)	1.17 (1.01-1.36)	0.04
Multivariable-adjusted RR (95% CI) <sup>b</sup>	1 [Reference]	1.03 (0.54-1.95)	1.42 (0.83-2.43)	1.77 (1.00-3.11)	1.20 (1.02-1.40)	0.02

Abbreviations: BMI, body mass index; CI, confidence interval; RR, relative risk.

<sup>a</sup> Cumulative-average BMI was calculated as averages of BMI reported up until the current cycle. For example, cumulative-average BMI at 1993 is the average of BMI in 1989, 1991, and 1993. Lag BMI was calculated using BMI 4 years before each cycle. As an example, person-time and early-onset CRC accrued during 1995-1997 were analyzed according to BMI in 1991.

<sup>b</sup> Additionally adjusted for height (continuous), family history of CRC (yes/no), history of diabetes (yes/no), screening lower endoscopy within past 10 years (yes/no), lower endoscopy due to other indications within past 10 years (yes/no), smoking pack-years (continuous), physical activity (continuous), alcohol intake (continuous), regular use of aspirin (yes/no), NSAID (yes/no), multivitamin (yes/no), menopausal status (premenopausal or postmenopausal), menopausal hormone use (never, past, and current use of menopausal hormones), and dietary intake (total calories, red meat, fiber, folate, calcium, Alternate Healthy Eating Index 2010, continuous).

<sup>c</sup> Calculated using cumulative average BMI as a continuous variable.

**eTable 3. Current BMI and risk of early-onset colorectal cancer according to tumor characteristics**

	Current BMI				<i>P</i> -trend <sup>b</sup>
	18.5-22.9 kg/m <sup>2</sup>	23-24.9 kg/m <sup>2</sup>	25-29.9 kg/m <sup>2</sup>	≥ 30 kg/m <sup>2</sup>	
<b>Colon cancer</b>					
Cases	21	15	21	23	
Person-years	452,256	217,277	296,770	230,180	
Age-adjusted RR (95% CI)	1 [Reference]	1.32 (0.68-2.57)	1.29 (0.70-2.37)	1.71 (0.94-3.11)	0.07
Multivariable-adjusted RR (95% CI) <sup>a</sup>	1 [Reference]	1.38 (0.71-2.69)	1.34 (0.72-2.49)	1.75 (0.93-3.28)	0.07
<b>Rectal cancer</b>					
Cases	8	5	9	12	
Person-years	452,270	217,282	296,782	230,184	
Age-adjusted RR (95% CI)	1 [Reference]	1.13 (0.37-3.46)	1.42 (0.54-3.69)	2.23 (0.90-5.50)	0.06
Multivariable-adjusted RR (95% CI) <sup>a</sup>	1 [Reference]	1.14 (0.37-3.52)	1.38 (0.52-3.66)	2.20 (0.85-5.66)	0.07
<b>Diagnosis between 1989-2001</b>					
Cases	21	13	19	18	
Person-years	370,782	167,513	218,268	160,524	
Age-adjusted RR (95% CI)	1 [Reference]	1.25 (0.62-2.50)	1.33 (0.71-2.49)	1.58 (0.83-2.98)	0.26
Multivariable-adjusted RR (95% CI) <sup>a</sup>	1 [Reference]	1.32 (0.66-2.65)	1.40 (0.74-2.63)	1.72 (0.89-3.34)	0.17
<b>Diagnosis after 2001</b>					
Cases	8	7	11	17	
Person-years	81,468	49,758	78,495	69,645	
Age-adjusted RR (95% CI)	1 [Reference]	1.34 (0.48-3.70)	1.35 (0.54-3.38)	2.38 (1.02-5.53)	0.007
Multivariable-adjusted RR (95% CI) <sup>a</sup>	1 [Reference]	1.40 (0.50-3.90)	1.37 (0.54-3.45)	2.24 (0.93-5.43)	0.02

Abbreviations: BMI, body mass index; CI, confidence interval; RR, relative risk.

<sup>a</sup> Additionally adjusted for height (continuous), family history of CRC (yes/no), history of diabetes (yes/no), screening lower endoscopy within past 10 years (yes/no), lower endoscopy due to other indications within past 10 years (yes/no), smoking pack-years (continuous), physical activity (continuous), alcohol intake (continuous), regular use of aspirin (yes/no), NSAID (yes/no), multivitamin (yes/no), menopausal status (premenopausal or postmenopausal), menopausal hormone use (never, past, and current use of menopausal hormones), and dietary intake (total calories, red meat, fiber, folate, calcium, Alternate Healthy Eating Index 2010, continuous).

<sup>b</sup> Calculated using current BMI as a continuous variable.

**eTable 4. Current BMI and risk of early-onset colorectal cancer according to smoking status and physical activity level**

	Current BMI				<i>P</i> -trend <sup>b</sup>
	18.5-22.9 kg/m <sup>2</sup>	23-24.9 kg/m <sup>2</sup>	25-29.9 kg/m <sup>2</sup>	≥ 30 kg/m <sup>2</sup>	
<b>Smoking status</b>					
Never smokers					
Cases	22	14	17	22	
Person-years	307,796	144,486	197,369	154,690	
Age-adjusted RR (95% CI)	1 [Reference]	1.20 (0.61-2.35)	1.01 (0.53-1.92)	1.57 (0.86-2.86)	0.08
Multivariable-adjusted RR (95% CI) <sup>a</sup>	1 [Reference]	1.33 (0.67-2.62)	1.11 (0.58-2.12)	1.72 (0.91-3.25)	0.06
Ever smokers					
Cases	7	6	13	13	
Person-years	144,454	72,785	99,394	75,479	
Age-adjusted RR (95% CI)	1 [Reference]	1.56 (0.52-4.66)	2.33 (0.92-5.90)	2.91 (1.14-7.38)	0.04
Multivariable-adjusted RR (95% CI) <sup>a</sup>	1 [Reference]	1.67 (0.55-5.04)	2.22 (0.87-5.67)	2.76 (1.04-7.33)	0.06
<b>Physical activity</b>					
4 <sup>th</sup> and 5 <sup>th</sup> quintiles (higher activity)					
Cases	14	9	12	14	
Person-years	212,298	93,357	115,595	69,270	
Age-adjusted RR (95% CI)	1 [Reference]	1.28 (0.55-2.97)	1.38 (0.63-3.03)	2.31 (1.07-5.00)	0.04
Multivariable-adjusted RR (95% CI) <sup>a</sup>	1 [Reference]	1.34 (0.57-3.16)	1.42 (0.64-3.17)	2.35 (1.05-5.25)	0.07
1 <sup>st</sup> to 3 <sup>rd</sup> quintiles (lower activity)					
Cases	15	11	18	21	
Person-years	239,952	123,914	181,168	160,899	
Age-adjusted RR (95% CI)	1 [Reference]	1.29 (0.59-2.80)	1.32 (0.66-2.65)	1.66 (0.84-3.21)	0.06
Multivariable-adjusted RR (95% CI) <sup>a</sup>	1 [Reference]	1.35 (0.62-2.97)	1.33 (0.66-2.66)	1.65 (0.80-3.20)	0.07

Abbreviations: BMI, body mass index; CI, confidence interval; RR, relative risk.

<sup>a</sup> Additionally adjusted for height (continuous), family history of CRC (yes/no), history of diabetes (yes/no), screening lower endoscopy within past 10 years (yes/no), lower endoscopy due to other indications within past 10 years (yes/no), smoking pack-years (continuous), physical activity (continuous), alcohol intake (continuous), regular use of aspirin (yes/no), NSAID (yes/no), multivitamin (yes/no), menopausal status (premenopausal or postmenopausal), menopausal hormone use (never, past, and current use of menopausal hormones), and dietary intake (total calories, red meat, fiber, folate, calcium, Alternate Healthy Eating Index 2010, continuous).

<sup>b</sup> Calculated using current BMI as a continuous variable.

**eTable 5. BMI at age 18, change in body weight since age 18, and risk of early-onset colorectal cancer**

Multivariable-adjusted RR of early-onset CRC (95% CI) <sup>a</sup>	Change in body weight since age 18			
	Gain < 5 kg or weight loss	Gain 5-19.9 kg	Gain ≥ 20 kg	
BMI at age 18	< 21 kg/m <sup>2</sup>	1 [Reference]	0.85 (0.41-1.76)	1.80 (0.82-3.91)
	21-22.9 kg/m <sup>2</sup>	0.86 (0.30-2.49)	1.36 (0.58-3.19)	2.20 (0.93-5.18)
	≥ 23 kg/m <sup>2</sup>	1.82 (0.78-4.22)	1.31 (0.51-3.35)	2.35 (1.05-5.25)

Abbreviations: BMI, body mass index; CI, confidence interval; CRC, colorectal cancer; RR, relative risk.

<sup>a</sup> Adjusted for age, questionnaire cycle, height (continuous), family history of CRC (yes/no), history of diabetes (yes/no), screening lower endoscopy within past 10 years (yes/no), lower endoscopy due to other indications within past 10 years (yes/no), smoking (continuous pack-years), physical activity (continuous), alcohol intake (continuous), regular use of aspirin (yes/no), NSAID (yes/no), multivitamin (yes/no), menopausal status (premenopausal or postmenopausal), menopausal hormone use (never, past, and current use of menopausal hormones), and dietary intake (total calories, red meat, fiber, folate, calcium, Alternate Healthy Eating Index 2010, continuous).

**eTable 6. Body shape at age 5, 10, and 20 and risk of early-onset colorectal cancer**

	Body Shape (Pictogram)			
	Average < 2.9	Average 3-3.9	Average ≥ 4	P-trend <sup>c</sup>
<b>Average body shape at age 5, 10, 20</b>				
Cases	50	39	22	
Person-years	611,212	344,550	214,446	
Age-adjusted RR (95% CI)	1 [Reference]	1.40 (0.92-2.13)	1.22 (0.74-2.03)	0.17
Multivariable-adjusted RR (95% CI) <sup>a</sup>	1 [Reference]	1.37 (0.89-2.09)	1.12 (0.67-1.87)	0.33
Multivariable-adjusted RR (95% CI) <sup>a, b</sup>	1 [Reference]	1.31 (0.86-2.01)	1.02 (0.61-1.72)	0.52
<b>Average body shape at age 10 and 20</b>				
Cases	41	38	32	
Person-years	536,131	358,462	275,615	
Age-adjusted RR (95% CI)	1 [Reference]	1.39 (0.89-2.16)	1.50 (0.94-2.39)	0.10
Multivariable-adjusted RR (95% CI) <sup>a</sup>	1 [Reference]	1.37 (0.88-2.14)	1.39 (0.87-2.23)	0.23
Multivariable-adjusted RR (95% CI) <sup>a, b</sup>	1 [Reference]	1.33 (0.85-2.08)	1.27 (0.79-2.06)	0.40
<b>Body shape at age 20</b>				
Cases	21	42	48	
Person-years	326,383	453,435	390,390	
Age-adjusted RR (95% CI)	1 [Reference]	1.44 (0.85-2.43)	1.94 (1.16-3.24)	0.05
Multivariable-adjusted RR (95% CI) <sup>a</sup>	1 [Reference]	1.44 (0.85-2.44)	1.85 (1.10-3.12)	0.13
Multivariable-adjusted RR (95% CI) <sup>a, b</sup>	1 [Reference]	1.39 (0.82-2.35)	1.71 (1.01-2.89)	0.23

Abbreviations: BMI, body mass index; CI, confidence interval; RR, relative risk. Participants who did not report their body shape were excluded in this analysis. Pictograms are graphical representation of body shape, ranging from 1 (most lean) to 9 (most overweight).

<sup>a</sup> Additionally adjusted for height (continuous), family history of CRC (yes/no), history of diabetes (yes/no), screening lower endoscopy within past 10 years (yes/no), lower endoscopy due to other indications within past 10 years (yes/no), smoking pack-years (continuous), physical activity (continuous), alcohol intake (continuous), regular use of aspirin (yes/no), NSAID (yes/no), multivitamin (yes/no), menopausal status (premenopausal or postmenopausal), menopausal hormone use (never, past, and current use of menopausal hormones), and dietary intake (total calories, red meat, fiber, folate, calcium, Alternate Healthy Eating Index 2010, continuous).

<sup>b</sup> Additionally adjusted for weight change since age 18.

<sup>c</sup> Calculated using (average) pictogram as a continuous variable.

**eTable 7. Change in body shape and risk of early-onset colorectal cancer**

	Change in Pictogram				P-trend <sup>c</sup>
	Decrease	Remain stable	Increase 1 grade	Increase ≥ 2 grades	
<b>Change from age 5 to age 20</b>					
Cases	17	27	37	30	
Person-years	149,838	345,848	437,225	237,298	
Age-adjusted RR (95% CI)	1.45 (0.79-2.67)	1 [Reference]	1.09 (0.66-1.79)	1.66 (0.98-2.79)	0.25
Multivariable-adjusted RR (95% CI) <sup>a</sup>	1.42 (0.77-2.61)	1 [Reference]	1.09 (0.66-1.80)	1.60 (0.94-2.71)	0.27
Multivariable-adjusted RR (95% CI) <sup>a, b</sup>	1.42 (0.77-2.62)	1 [Reference]	1.06 (0.64-1.75)	1.42 (0.79-2.56)	0.66
<b>Change from age 10 to age 20</b>					
Cases	18	38	39	16	
Person-years	207,875	383,981	441,427	136,924	
Age-adjusted RR (95% CI)	0.87 (0.50-1.53)	1 [Reference]	0.90 (0.57-1.40)	1.19 (0.66-2.14)	0.48
Multivariable-adjusted RR (95% CI) <sup>a</sup>	0.84 (0.48-1.47)	1 [Reference]	0.89 (0.57-1.40)	1.14 (0.63-2.07)	0.48
Multivariable-adjusted RR (95% CI) <sup>a, b</sup>	0.83 (0.47-1.47)	1 [Reference]	0.85 (0.54-1.34)	0.96 (0.50-1.83)	0.84

Abbreviations: BMI, body mass index; CI, confidence interval; RR, relative risk. Participants who did not report their body shape were excluded in this analysis.

Pictograms are graphical representation of body shape, ranging from 1 (most lean) to 9 (most overweight).

<sup>a</sup> Additionally adjusted for height (continuous), family history of CRC (yes/no), history of diabetes (yes/no), screening lower endoscopy within past 10 years (yes/no), lower endoscopy due to other indications within past 10 years (yes/no), smoking pack-years (continuous), physical activity (continuous), alcohol intake (continuous), regular use of aspirin (yes/no), NSAID (yes/no), multivitamin (yes/no), menopausal status (premenopausal or postmenopausal), menopausal hormone use (never, past, and current use of menopausal hormones), and dietary intake (total calories, red meat, fiber, folate, calcium, Alternate Healthy Eating Index 2010, continuous).

<sup>b</sup> Additionally adjusted for pictogram at age 20.

<sup>c</sup> Calculated using change in pictogram as a continuous variable.



**eTable 8. BMI, weight change, and risk of colorectal cancer after age 50**

	Current BMI						
	18.5-22.9 kg/m <sup>2</sup>	23-24.9 kg/m <sup>2</sup>	25-29.9 kg/m <sup>2</sup>	≥ 30 kg/m <sup>2</sup>	Each 5 kg/m <sup>2</sup> increase	P-trend <sup>b</sup>	P-heterogeneity <sup>c</sup>
Cases	34	33	43	45			0.01
Person-years	569,181	302,580	453,386	379,939			
Age-adjusted model	1 [Reference]	1.35 (0.83-2.18)	0.93 (0.59-1.46)	0.98 (0.62-1.53)	0.96 (0.84-1.09)	0.49	
Multivariable-adjusted model <sup>a</sup>	1 [Reference]	1.37 (0.84-2.22)	0.93 (0.58-1.47)	0.94 (0.58-1.52)	0.94 (0.81-1.08)	0.38	
	BMI at age 18						
	< 18.5 kg/m <sup>2</sup>	18.5-20.9 kg/m <sup>2</sup>	21-22.9 kg/m <sup>2</sup>	≥ 23 kg/m <sup>2</sup>	Each 5 kg/m <sup>2</sup> increase	P-trend <sup>b</sup>	
Cases	14	63	36	42			
Person-years	212,887	730,278	396,294	365,627			
Age-adjusted model	0.76 (0.43-1.36)	1 [Reference]	1.07 (0.71-1.61)	1.37 (0.93-2.03)	1.18 (0.94-1.47)	0.15	
Multivariable-adjusted model <sup>a</sup>	0.73 (0.41-1.30)	1 [Reference]	1.09 (0.72-1.65)	1.39 (0.93-2.08)	1.19 (0.94-1.49)	0.14	
Multivariable-adjusted model <sup>a, d</sup>	0.74 (0.41-1.33)	1 [Reference]	1.10 (0.73-1.67)	1.38 (0.92-2.06)	1.15 (0.92-1.44)	0.23	
	Weight change since age 18						
	Weight Loss or Weight Gain < 5 kg <sup>d</sup>	Weight Gain 5 – 19.9 kg	Weight Gain 20 – 39.9 kg	Weight Gain ≥ 40 kg	Each 5 kg Increase	P-trend <sup>b</sup>	
Cases	36	64	41	14			
Person-years	465,657	788,880	362,771	87,778			
Age-adjusted model	1 [Reference]	0.73 (0.49-1.11)	0.71 (0.45-1.11)	0.82 (0.44-1.52)	0.91 (0.82-1.02)	0.11	
Multivariable-adjusted model <sup>a</sup>	1 [Reference]	0.72 (0.47-1.09)	0.67 (0.42-1.07)	0.70 (0.36-1.36)	0.89 (0.79-1.00)	0.05	
Multivariable-adjusted model <sup>a, e</sup>	1 [Reference]	0.76 (0.49-1.16)	0.70 (0.44-1.13)	0.72 (0.37-1.40)	0.90 (0.80-1.01)	0.07	

Note: Relative risk and 95% confidence interval is shown. Simple-updated BMI is used. BMI, body mass index.

<sup>a</sup> Additionally adjusted for height (continuous), family history of CRC (yes/no), history of diabetes (yes/no), screening lower endoscopy within past 10 years (yes/no), lower endoscopy due to other indications within past 10 years (yes/no), smoking pack-years (continuous), physical activity (continuous), alcohol intake (continuous), regular use of aspirin (yes/no), NSAID (yes/no), multivitamin (yes/no), menopausal status (premenopausal or postmenopausal), menopausal hormone use (never, past, and current use of menopausal hormones), and dietary intake (total calories, red meat, fiber, folate, calcium, Alternate Healthy Eating Index 2010, continuous).

<sup>b</sup> Calculated using current BMI, BMI at age 18, and weight change since age 18 as a continuous variable.

<sup>c</sup> Calculated using the log likelihood ratio test comparing models assuming a common effect between obesity and risk of CRC with models allowing separate associations between obesity and risk of CRC according to age strata (<50/≥50 years). The median follow-up duration for the cohort was 20.8 years.

<sup>d</sup> Additionally adjusted for weight change since age 18.

<sup>e</sup> Additionally adjusted for BMI at age 18.

**eFigure 1.** Non-parametric restricted cubic splines of (A) current BMI, (B) BMI at age 18, and (C) weight change since age 18 and risk of early-onset colorectal cancer. Dotted lines represent 95% confidence intervals.

