

**Table 2.45. Case-control studies on smoking and risk of colorectal adenoma**

Reference, location, name of study	Characteristics of cases	Characteristics of controls	Smoking categories	Relative risks (95%CI or <i>p</i> value)			Adjustment factors/ comments
				Colorectal adenomas	Hyperplastic polyps	Concurrent hyperplastic polyps and adenomas	
Hoshiyama et al. (2000) Japan	105 patients with newly diagnosed colon adenoma Total colonoscopy between 1992 and 1994, Self-administered questionnaire	843 general population controls and 84 hospital controls who had no pathologic lesions at colonoscopy	Comparison with population controls:				Adjusted for age and sex
			<i>Smoking status</i>				
			Ex	1.81 (0.95-3.45)			
			Current	1.54 (0.88-2.71)			
			<i>Cigarette years</i>				
			Nonsmoker				
			≤800	1.68 (0.98-2.90)			
			>800	1.42 (0.68-2.94)			
			Comparison with hospital controls:				
			<i>Smoking status</i>				
Ex	1.53 (0.61-3.84)						
Current	2.86 (1.21-6.80)						
<i>Cigarette years</i>							
≤800	2.01 (0.93-4.32)						
>800	3.62 (0.89-14.73)						
Ulrich et al. (2001) USA	Cases diagnosed at Minnesota Cancer Preventioin Research Unit; 530 confirmed adenomas, 202 hyperplastic polyps; ages 30 to 74 years; colonoscopy between April 1991 and April 1994; participation rate for colonoscopy patients was 68%; only with complete colonoscopy eligible	649 controls polyp-free at colonoscopy	<i>Smoking status</i>				Adjusted for age, sex, regular use of nonsteroidal anti-inflammatory drugs, hormone-replacement therapy, alcohol consumption, total calories, body mass index and dietary fiber
			Former smoker	1.4 (1.0-1.9)	2.3(1.5-3.6)		
			Current smoker	2.1 (1.5-3.1)	4.3(2.6-7.0)		
			<i>Pack-years</i>				
			≤25	1.9 (1.3-2.7)	3.2(1.9-5.4)		
			>25	2.0 (1.4-2.8)	3.7(2.4-5.9)		
			<i>Among ex-smokers:</i>				
			yrs since quitting				
			1-9	1.0	1.0		
			10-19	1.0 (0.6-1.7)	0.8(0.4-1.5)		
20+	0.7 (0.5-1.2)	0.6(0.3-1.1)					

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Erhardt et al (2002) Germany	Patients reporting for colonoscopy at the Robert-Bosch Hospital Stuttgart; 502 Caucasian subjects with complete colonoscopy, 207 with colorectal adenomas, 71 with hyperplastic polyps	224 controls free of polyps	Ever smoker p trend	1.56 (1.01-2.39) 0.043	1.79(1.04-3.06) 0.035		Adjusted for age, sex, BMI,
Tiemersma et al. (2004) Netherlands	431 adenoma cases (54% women) enrolled at endoscopy in 8 Dutch hospitals between 1997 and 2000; subjects aged between 18-75 years; response was 54%; complete visualization of the colon was achieved for 78% of controls and 89% of cases	432 polyp-free controls	<i>Smoking status</i> Former Current <i>Duration of smoking</i> 1-15 16-25 >25 p trend <i>Cigarettes per day</i> 1-9 10-19 ≥20 p trend <i>Time since quitting (years)</i> >18 8.1-18 1-8 <1 p trend	1.62 (1.12-2.33) 2.10 (1.38-3.18) 1.28 (0.70-2.33) 2.19 (1.21-3.98) 2.42 (1.43-4.11) 0.0006 1.09 (0.56-2.13) 0.89 (0.44-1.79) 1.17 (0.59-2.33) 0.78 1.23 (0.73-2.07) 1.26 (0.70-2.27) 2.06 (1.18-3.59) 2.13 (1.42-3.21) 0.03			Adjusted for age, sex, indication of endoscopy and consumption of snacks and alcohol. ORs for smoking duration were additionally adjusted for the number of cigarettes smoked per day(continuous); ORs for cigarettes per day were additionally adjusted for smoking duration in years (continuous)

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Toyomura et al. (2004) Japan	Men of Self Defence Forces (SDF) with total or partial colonoscopy at preretirement between 1995-2002 at 2 hospitals; 754 cases with histologically proven colorectal adenomas	1547 controls with normal colonoscopy	<i>Colorectum</i>				
			Cigarette years;				
			1-399	1.2 (0.9-1.6)			
			400-799	1.9 (1.5-2.4)			
			≥800	2.3 (1.7-3.1)			
			Trend	p=0.0001			
			<i>Proximal colon</i>				
			1-399	1.0 (0.6-1.5)			
			400-799	1.7 (1.2-2.3)			
			≥800	2.1 (1.4-3.2)			
			Trend	p=0.0001			
			<i>Distal colon</i>				
			1-399	1.0 (0.7-1.5)			
			400-799	1.7 (1.2-2.7)			
			≥800	1.8 (1.2-2.7)			
			Trend	p=0.0003			
			<i>Rectum</i>				
			1-399	2.5 (1.1-5.4)			
			400-799	2.3 (1.1-4.7)			
			≥800	5.6 (2.6-11.9)			
Trend	p=0.0001						
<i>Colorectum Small (&lt;5mm)</i>							
1-399	1.0 (0.7-1.3)						
400-799	1.6 (1.2-2.1)						
≥800	2.0 (1.4-2.9)						
Trend	p=0.0001						
<i>Large (≥5mm)</i>							
1-399	1.7 (1.1-2.7)						
400-799	2.5 (1.7-3.6)						
≥800	3.4 (2.2-5.3)						
Trend	p=0.0001						
<i>Single polyp</i>							
1-399	1.0 (0.7-1.4)						
400-799	1.2 (0.9-1.6)						
≥800	1.7 (1.2-2.4)						
Trend	p=0.015						

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Toyomura et al. (2004) (contd)		1547 controls with normal colonoscopy	<i>Multiple polyps</i> 1-399 400-799 ≥800 Trend	1.5 (1.0-2.3) 3.1 (2.2-4.2) 3.6 (2.4-5.3) p=0.0001			Adjusted for rank, hospital, body mass index, physical activity, and alcohol intake
Tranah et al. (2004) USA (NHS) (HPFS)	Nested case-control studies in the Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS). 556 incident cases (NHS); 376 prevalent cases (HPFS); NHS: Case or control must have undergone sigmoidoscopy or colonoscopy; HPFS: Participant reported a diagnosis of colorectal adenoma on follow-up questionnaires, cases confirmed by histopathological reports reviewed by a study investigator	557 controls (NHS) or 725 controls (HPFS); NHS: One control matched to each case on year of birth, month of blood draw, fasting status, time period of endoscopy and routine screening, gastrointestinal symptoms or family history of colorectal cancer ; HPFS: Two controls matched to each case on year of birth, year of endoscopy and whether they had had a previous endoscopy	<i>Pack years smoking</i> NHS <25 years ≥25 years  HPFS <25 years ≥25 years	1.06 (0.80-1.41) 1.40 (1.03-1.91)  1.40 (1.02-1.92) 1.87 (1.32-2.63)			

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Ji et al (2006) USA	Participants randomized to the screening arm of the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial; 4383 cases with pathologically verified polyps of the distal colon, including 1545 cases with hyperplastic polyps only, 2339 cases with adenoma only and 499 cases with both hyperplastic polyps and adenoma	33667 controls colonoscopy negative for distal colon polyps	<i>Smoking status</i>				Adjusted for age, sex, education, alcohol intake, fruit, and study centers, boiled
			Current smoker	1.8 (1.5-2.1)	4.4 (3.7-5.2)	6.2 (4.7-8.3)	
			Ex smokers	1.1 (1.0-1.2)	1.8 (1.6-2.1)	2.2 (1.7-2.8)	
			<i>Cigarettes per day</i>				
			1-10	1.1 (1.0-1.3)	1.6 (1.3-1.9)	2.0 (1.5-2.8)	
			11-20	1.2 (1.1-1.3)	2.2 (1.9-2.5)	2.8 (2.2-3.7)	
			21-30	1.3 (1.1-1.5)	2.7 (2.3-3.2)	3.4 (2.5-4.6)	
			≥31	1.3 (1.1-1.5)	2.6 (2.2-3.1)	2.9 (2.1-4.0)	
			<i>p</i> trend	0.04	<0.0001	0.05	
			<i>Smoking duration (y)</i>				
			<15	1.0 (0.8-1.1)	1.2 (1.0-1.4)	1.2 (0.8-1.7)	
			15-24	1.0 (0.9-1.2)	1.4 (1.1-1.7)	1.8 (1.3-2.5)	
			25-34	1.2 (1.1-1.4)	2.4 (2.1-2.9)	2.6 (1.9-3.5)	
			35-44	1.5 (1.3-1.7)	3.5 (3.0-4.1)	4.3 (3.3-5.7)	
			≥45+	1.8 (1.5-2.2)	4.2 (3.4-5.1)	7.2 (5.2-10.0)	
			<i>p</i> trend	<0.0001	<0.0001	<0.0001	
			<i>Pack years</i>				
			1-9	1.0 (0.9-1.2)	1.4 (1.2-1.6)	1.5 (1.1-2.1)	
			10-19	1.1 (1.0-1.3)	1.7 (1.4-2.0)	1.9 (1.4-2.8)	
			20-29	1.1 (0.9-1.3)	2.3 (1.9-2.8)	2.8 (2.0-4.0)	
			30-39	1.4 (1.2-1.7)	3.2 (2.6-3.8)	4.7 (3.5-6.5)	
			40-54	1.5 (1.3-1.8)	3.5 (2.9-4.3)	3.7 (2.5-5.3)	
			≥55	1.6 (1.4-1.9)	3.7 (3.0-4.5)	4.8 (3.4-6.6)	
<i>p</i> trend	<0.0001	<0.0001	<0.0001				
<i>Years since stopped smoking (y)</i>							
≥40	1.0 (0.7-1.3)	1.2 (0.8-1.7)	1.3 (0.7-2.4)				
30-<40	0.9 (0.8-1.1)	1.3 (1.0-1.6)	1.2 (0.8-1.8)				
20-<30	1.0 (0.9-1.2)	1.3 (1.1-1.6)	1.5 (1.1-2.2)				
10-<20	1.2 (1.1-1.4)	2.2 (1.8-2.6)	2.6 (1.9-3.5)				
<10	1.4 (1.2-1.7)	3.3 (2.8-3.9)	4.4 (3.2-5.9)				
<i>p</i> trend	<0.0001	<0.0001	<0.0001				

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				Colorectal adenomas	Hyperplastic polyps	Concurrent hyperplastic polyps and adenomas	
Larsen et al. (2006) Norway (NORCCAP)	The Norwegian Colorectal Cancer Prevention study (NORCCAP) – a cross sectional study within a randomized controlled colorectal cancer screening trial (n=6961); men and women born between 1946-1950; response rate among attendees was 97%; 443 low-risk adenomas and 108 “advanced neoplasia”	3447 controls sigmoidoscopy negative	<i>Smoking status</i> Former Occasional <i>Cigarettes per day</i> 1-10 cigarettes/day 11-20 cigarettes/day >20 cigarettes/day p trend	<i>Low-risk adenomas</i>  1.06 (0.79-1.41) 1.29 (0.78-2.15) 1.30 (0.93-1.83) 1.76 (1.29-2.40) 1.43 (0.77-2.65) <0.001			Adjusted for gender, age, BMI, smoking habits, total score for exercise, total consumption of vegetables, fruit and berries, boiled potatoes, poultry, other meat than poultry and fatty fish.
Stern et al (2006) USA	A sigmoidoscopy-based case-control study in Los Angeles County; study subjects examined 1991-1993 (phase I) and 1993 to 1995 (phase II); 735 cases with a first-time diagnosis of histologically confirmed adenoma	799 controls were subjects with no current or past polyps, individually matched to cases by gender, age (within 5 years) sigmoidoscopy date (within 3 months) and center	<i>Smoking status</i> Former Current <i>Years of smoking</i> >0-26 >26 p trend <i>Pack-years smoking</i> >0-21 >21 p trend	1.2 (1.0-1.6) 2.2 (1.6-3.0) 1.1 (0.8-1.4) 1.8 (1.4-2.3) <0.001 1.1 (0.9-1.4) 1.7 (1.3-2.2) <0.001			Adjusted for age at diagnosis, sex, race, clinic, and exam date.

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Shrubsole et al. (2008) USA Tennessee Colorectal Polyp Study	Tennessee Colorectal Polyp Study, an ongoing colonoscopy-based case-control study in Nashville, Tennessee; eligible participants aged 40-75 years, identified between 2003 and 2005, 67% provided an written informed consent and participated; 299 cases with hyperplastic polyps, 639 cases with adenomatous polyps, 234 cases with both adenomatous and hyperplastic polyps	Controls had complete colonoscopy 1773 polyp-free controls	<i>Smoking status</i>				Adjusted for age, sex, study site, year, recruitment type (pre- or post-colonoscopy), body mass index, height, indication for colonoscopy, educational level, race/ethnicity, family history of cancer and polyps, use of non-steroidal anti-inflammatory drugs; physical activity, menopausal status, daily intakes of fruits and vegetables, dairy foods and meat, and alcohol drinking
			Pipe/other tobacco user only	1.2 (0.7-2.1)	1.2 (0.5-2.9)	1.1 (0.4-3.4)	
			Former cig. smoker	1.1 (0.9-1.4)	1.5 (1.1-2.2)	2.8 (1.8-4.3)	
			Current cig. smoker	1.8 (1.3-2.5)	4.8 (3.3-7.1)	7.7 (4.7-2.4)	
			<i>p</i> trend	0.003	<0.0001	<0.0001	
			<i>Cigarettes per day</i>				
			<20	1.3 (1.0-1.7)	2.1 (1.5-3.1)	3.2 (2.0-5.0)	
			20-29	1.2 (0.8-1.6)	2.2 (1.5-3.2)	4.1 (2.6-6.5)	
			≥30	1.3 (1.0-1.7)	2.5 (1.7-3.8)	4.5 (2.8-7.2)	
			<i>p</i> trend	0.09	<0.0001	<0.0001	
			<i>Years of smoking</i>				
			<15	0.8 (0.6-1.2)	0.7 (0.4-1.3)	2.0 (1.2-3.5)	
			15-<25	1.1 (0.8-1.5)	2.1 (1.3-3.3)	2.7 (1.5-4.7)	
			25-<35	1.4 (1.0-2.0)	2.8 (1.8-4.2)	5.0 (3.0-8.2)	
			≥35	1.9 (1.4-2.5)	5.0 (3.3-7.3)	6.9 (4.4-11.1)	
			<i>p</i> trend	<0.001	<0.0001	<0.0001	
			<i>Pack-years</i>				
			<10	1.0 (0.8-1.4)	1.2 (0.7-1.8)	1.9 (1.1-3.2)	
			10-<30	1.2 (0.9-1.7)	2.6 (1.8-3.8)	3.5 (2.2-5.7)	
			≥30	1.5 (1.1-2.0)	3.1 (2.1-4.5)	6.2 (4.0-9.7)	
<i>p</i> trend	0.003	<0.0001	<0.0001				
<i>Age at starting to smoke</i>							
<18	1.2 (0.9-1.5)	2.1 (1.5-3.0)	3.3 (2.2-5.1)				
18-20	1.3 (1.0-1.7)	2.7 (1.9-3.9)	4.5 (2.9-7.0)				
≥21	1.3 (0.9-1.8)	2.3 (1.5-3.7)	2.7 (1.5-4.8)				
<i>p</i> trend	0.09	<0.0001	<0.0001				
<i>Years since quitting</i>							
<10	1.0 (0.7-1.5)	0.6 (0.4-1.0)	0.7 (0.4-1.1)				
10-19	0.7 (0.5-1.1)	0.4 (0.3-0.6)	0.4 (0.3-0.7)				
≥20	0.4 (0.3-0.6)	0.2 (0.1-0.3)	0.2 (0.2-0.4)				
Never smoker	0.5 (0.4-0.7)	0.2 (0.1-0.3)	0.1 (0.1-0.2)				
<i>p</i> trend	<0.0001	<0.0001	<0.0001				

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				Colorectal adenomas	Hyperplastic polyps	Concurrent hyperplastic polyps and adenomas	
Hermann et al. (2009) Germany, EPIC	Participants of EOIC-Heidelberg cohort, 25540 participants aged 35 and 65 years recruited 1994-1998; self reported diagnosis of benign tumors such as colorectal polyps; colorectal polyps were verified by a trained physician using medical record; 536 incident colorectal adenoma, 167 hyperplastic polyps	3966 controls with negative colonoscopy	<i>Smoking status</i>				Adjusted for age at baseline, sex, energy intake, total red and processed meat intake, intake of milk and milk products, fiber intake, folate intake, family history of colorectal cancer, education
			Former	1.17 (0.94-1.45)			
			Current	1.40 (1.06-1.84)			
			Men				
			Former	1.06 (0.81-1.39)			
			Current	1.00 (0.68-1.46)			
			Women				
			Former	1.27 (0.88-1.83)			
			Current	2.06 (1.39-3.08)			
			p interaction	0.02			
			<i>Pack years</i>				
			0.076 to ≤5	0.96 (0.71-1.30)			
			5 to ≤10	1.26 (0.90-1.75)			
			10 to ≤15	1.32 (0.93-1.87)			
			>15	1.45 (1.14-1.84)			
			p trend	0.001			
			Men				
0.076 to ≤5	0.75 (0.50-1.13)						
5 to ≤10	0.96 (0.62-1.50)						
10 to ≤15	1.06 (0.69-1.64)						
>15	1.18 (0.88-1.59)						
p trend	0.17						
Women							
0.076 to ≤5	1.29 (0.81-2.04)						
5 to ≤10	1.78 (1.08-2.94)						
10 to ≤15	1.87 (1.03-3.38)						
>15	2.05 (1.34-3.13)						
p trend	0.0002						
p interaction	0.003						