Table 2.19. Case–control studies of *helicobacter pylori* infection and colorectal cancer

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk* (95% CI)	Adjusted potential confounders	Comments
Penman *et al* (1994) Scotland, UK	42 sporatic colorectal neoplasia (40 carcinoma, 2 severely dysplastic adenomas) selected from a total of 120. Exclusions included too ill, history of familial adenomatous polyposis or intestinal obstruction and emergency surgery.	34 age and sex matched in-patients awaiting elective surgery under general anesthesia for minor conditions. Exclusion included history of malignancy at any other site, treatment with acid-suppressing drugs, previous peptic ulcer surgery, documented pernicious anemia, renal failure, hypercalcemia, recent antibiotic therapy (1 week) or any form of bowel prep in the two days before study tests. These exclusions applied to cases as well as controls.	[^{14}C] urea breath test and serology ELISA IgG *H.pylori* antibodies.	*Breath test Positive*	25	1.31 (0.53-3.23)	None	RR not reported in manuscript. Crude RR computed.
				Serology Positive	24	1.33(0.54-3.28)		

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Moss *et al* (1995) USA	41 cases of colorectal cancer; 49% male; mean age 68± 13yrs., aged 30-90; 86% white, 7% black, 2% Hispanic, 5% other: 73% social class I/II. Cases diagnosed 1988-92.	All controls underwent colonoscopy at the same private surgical practice as cases. 41 with adenomatous polyps; 51% male; mean age 67± 13, aged 21-87; 86% white, 7% black, 2% Hispanic, 5% other; 91% social class I/II. 41 endoscopically normal ; 49% male; mean age 65± 11 aged, aged 31-8; 86% white, 7% black, 2% Hispanic, 5% other; 91% social class I/II.	Serology/ELISA *H. pylori* IgG	*Cut point not specified H.pylori+*	23	Cases vs. polyp controls 1.00(0.37-2.70) Cases vs. normal controls 0.74(0.28-1.96)	None	Matched by age, sex, and race.
Meucci *et al* (1997) Italy	38 cases with colon cancer and 56 patients with colonic adenomas. Cancer cases: 64% men, age 62.0 years; age 62.0 years; age range 38-84. Polyp cases: 68% men; mean age 65.3; age range 35-81.	100 controls selected from patients in hematology clinic for anticoagulant therapy. Matched 2 to 1 on first 50 cases by age (± 3 years) and gender. 71% men; mean age 36.1 years; age range 37-81.	Serology/ELISA *H. pylori* IgG	*Positive >500 units*	Colon Cancer 21 Colon polyps 40 Cancer or polyps	1.28 (0.61-2.70) 2.6 (1.30-5.21) 1.92(1.08-3.41)	None	25 of 38 colon cancer cases were evaluated for *H.pylori* 1-9 years post colon surgery and may have biased the prevalence of *H. pylori* in cases downward.

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Fireman *et al* (2000) Israel	51 newly diagnosed histologically confirmed colorectal cancer patients. Exclusion criteria: history of colorectal cancer and/or colonic polyps chronic colon disease, IBD or lymphoma or peptic and duodenal disease in which *H.pylori* was detected. Age range 36-87; 28 males, 23 females. All subjects underwent endoscopy in 1997.	51 controls with no clinical evidence or history of peptic disease who underwent colonoscopy and gastroscopy with no pathology found. Same exclusion criteria as cases. Age range 20-93; 22 males, 29 females.	Serology/ELISA *H.pylori* IgG	*>7U Positive*	41	2.43(0.99-5.95)	None	RR not reported in manuscript. Crude RR computed.
			Urease test on antral mucosal biopsy.	*Positive*	17	0.70(0.29-1.69)		
Hartwich *et al* (2001) Poland	80 cases with histologically confirmed colorectal adenocarcinoma. Median age 64 years, age range 47-82; 65 men, 15 women	160 controls age and gender matched: 130 men, 30 women; median age 63 years, age range 47-82.	[^{13}C] urea breath test (UBT) and/or	*H.pylori* UBT+	52	1.41(0.81-2.45)	None	RR not reported in manuscript. Crude RR computed from estimated numbers exposed using reported percentages.
			Serology/ELISA *H.pylori* IgG	Serology *H.pylori+*	68	3.78(1.91-7.46)		
			ELISA CagA IgG	CagA+	48	3.50(2.00-6.12)		
Siddheshwar *et al* (2001) UK	189 cases of colorectal carcinoma. 57 patients with colorectal polyps.	179 controls that had undergone barium enema or colonoscopy.	Serology/ELISA *H. pylori* IgG	*H.pylori+*	Not reported	Cancer 1.1(0.7-1.8) Polyps 1.3(0.7-2.5)	Age, sex, social class (I-II, III, IV-V)	Age and sex were associated with *H.pylori* infection; however, patients in social classes IV and V were more likely to be infected than those in social classes I-III.

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Shmuely *et al* (2001) Israel	67 patients with histologically confirmed colorectal adenocarcinoma. Patients who had surgery or chemotherapy to treat cancer or therapy to eradicate *H. pylori* were excluded.	47 controls with other malignancies and 45 controls hospitalized for tranesophageal echocardiography (TEE controls, TEE controls excluded if they had underlying malignancy (self reported or chart) other malignancy controls excluded if treated with chemotherapy.	Serology/ELISA *H.pylori* IgG Anti CagA antibodies by Western blot (IgG against CagA)	*H.pylori*+ CagA+ Presence of 116 kd band	50 41	*H.pylori*+ vs. cancer controls 1.52 (0.68-3.41) vs. TEE controls 1.19(0.52-2.76) vs. pooled controls 1.35(0.67-2.72) CagA+ *H.pylori*+ vs. cancer controls 8.3(3.0-22.9) vs. TEE controls 6.7(2.5-18.0) vs. pooled controls 7.4(3.1-17.7)	None	Hospital based study, consecutive patients admitted between March 1999 and February 2000. All *H.pylori* negative cases and controls were also seronegative for CagA. All *H.pylori* RR not reported in manuscript Crude RR computed.

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Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk* (95% CI)	Adjusted potential confounders	Comments
Fujimori *et al* (2005) Japan 1996-2003	Cases identified from 669 male and female patients undergoing barium enema exam and total colonoscopy. Aged 40-80 years. Distribution by diagnosis: 327 adenoma patients, 154 adenocarcinoma patients; 481 patients with tumours (see comments).	Controls identified from 669 male and female cases undergoing barium enema exam and colonoscopy, aged 40 - 80 years, and free of colorectal ademomas and adenocarcenomas, n=188.	UBIT ^{13}C-urea breath test, rapid urease test by Helicocheck or histological diagnosis of biopsied gastric specimens.	*^{13}C-urea H.pylori negative <2.5%* *Positive ≥ 2.5%*	<u>All cases</u> Adenoma 264 Adenocarcinoma 127 Tumour 391 <u>Male cases</u> Adenoma 222 Adenocarcinoma 81 Tumour 303 <u>Female cases</u> Adenoma 42 Adenocarcinoma 46 Tumour 88	 1.60(1.18-2.02) 1.80(1.28-2.32) 1.66(1.27-2.05) 1.08(0.50-1.66) 1.52(0.74-2.30) 1.17(0.61-1.73) 1.68(0.96-2.40) 2.09(1.35-2.83) 1.87(1.27-2.47)	Age	Adenocarcinoma confined to adenoma was defined as adenoma. Pts. with either adenoma or adenocarcinoma classified as tumour. Cross sectional allocation of cases and controls.

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D'Onghia *et al* (2007) Italy	29 cases of colorectal cancer;17 (59%) men and 12 (41%) women; aged 51-84 years hospitilized patients from Department of Surgery. 19% Stage 1 adenocarcinoma. 38% Stage II and 43% Stage III. By tumor site 14 right colon, 7 left colon, 8 rectum.	50 health blood donors controls: 39 (78%) men and 11 (22%) women aged 32-65; 30% controls normal weight; 54% overweight; 16% obese.	Serology/ELISA anti *H.pylori* IgG	*Cutpoint not specified* *Positive*	13	1.33(0.53-3.32)	None	Poor match on age and gender. RR not reported in manuscript. Crude RR computed from available data.
Zumkeller *et al* (2007) Germany	384 of 540 incident colorectal adenocarcinoma cases: residents of study region, aged 30 and older, physically and mentally able to participate. Analysis restricted to subjects between 30 and 75 years of age. Distribution 220 (57%) colon cancer, 164 (43%) rectal cancer; 63% males; mean age, 64.0 years; age range 37-75. Diagnosed 2003-2004.	467 of 641 matched control subjects selected from population registers. Frequently matched to cases on 5 year age groups, gender, county of residence, no history of colorectal cancer (CRC) 58% male; mean age 63.5 years; age range 34-75.	Serology/ELISA anti *H.pylori* IgG; *H.pylori* CagA protein antibodies by [c]*H. pylori* p120 (CagA) ELISA kit	*H.pylori*+ CagA + *H.pylori* ++ CagA[-]	195 135 NR	1.41(1.06-1.87) 1.34 (0.98-1.84) 1.46(0.98-2.16)	Age, gender, education level, nationality, smoking status, average lifetime alcohol consumption, BMI, average lifetime physical activity score (MET), red meat and cold sausage consumption, red meat preparation, history of diabetes, intake of NSAIDS, regular use of female hormone replacement therapy, and history of CRC screening.	Population based study included 22 hospitals in southwest Germany. RR similar for colon cancer and rectal cancer cases.

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Jones *et al* (2007) U.K.	Paraffin –embedded colorectal tissue representing: 60 adenomatous polyp cases 60 adenocarcinoma cases Final series 59 adenocarcinoma cases: 37% men, 63% women; mean age 67.55 years; age range 36-91. Adenomas 20 villous 20 tubulovillous 19 tubular	Peraffin-embedded colorectal tissue: 60 normal tissue 58 included in analysis: 43% men, 57% women mean age 51.60 years; age range 22-86. No biopsy history of colorectal adenomas or carcinomas or other carcinoma.	H/E stained sections of paraffin embedded tissue and immunohisto-chemistry stained slides (polyclonal NCL-HPp dilution 1:800) Positivity for both antibodies was convergent.	Positive staining observed by light microscopy	Cancer cases 10 Adenoma cases Villous 1 Tubulovillous 4 Tubular 4	8.73 (1.01-75.48) 1.94(0.10-36.77) 5.73(1.02-112.83) 11.53(1.12-118.98)	Age and sex	Pilot study of *H.pylori* in tissue from colorectal neoplasms vs. normal colonic tissue. Specimens not matched for age, sex, or SES. No information available on serology breath test or previous gastric biopsy.

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Machida-Montani *et al* (2007) Japan	121 newly diagnosed colorectal cancer (CRC) cases diagnosed 10/1998-3/2002 at 4 hospitals in Nagano prefecture. 113 cases included in analysis: age range 20-70.	226 controls were participants of a health check-up program, matched to cases 2:1 by age (+ 3 years), gender and residence	Serology/ ELISA *H. pylori* IgG CagA IgG Helico G, Porton-Cambridge, Oxford UK; RADIM Rome IT	*H.pylori*+ > 10 U/ml CagA+ > 10 U/ml *H.pylori* infection+ (*H.pylori*+ and/or CagA+)	*H.pylori+* Colon 40 Rectum 34 Colorectum 74 CagA+ Colon 40 Rectum 29 Colorectum 69 H.pylori+ or CagA+ Colon 46 Rectum 36 Colorectum 82	 1.12 (0.59-2.14) 0.94(0.42-2.12) 1.06(0.65-1.74) 1.07(0.55-2.08) 0.71(0.33-1.56) 0.89(0.54-1.46) 1.25(0.63-2.49) 0.70(0.26-1.84) 1.00(0.58-1.74)	Smoking Status (never, past, current) BMI (continuous) Membership in agricultural cooperative	