

Table 2.9. Case-control studies of *helicobacter pylori* infection and oesophageal adenocarcinoma

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
Chow <i>et al</i> (1998) USA 1993-1995	129 cases of newly diagnosed oesophageal/gastric cardia (OGC) adenocarcinoma.	224 population controls selected by random digit dialing for those <65 years of age and from Health Care Financing Admin. Files for those ≥ 65 years. Frequency matched to cases by age, sex and race	Serology/ELISA Anti <i>H.pylori</i> IgG CagA status by ELISA serum IgG against on 220 (CagA proteins) CagA-AI<0.3	Anti <i>H.pylori</i> IgG (whole cell) seropositive $CagA^+ \geq 0.3$ $CagA^- < 0.3$	Not reported	CagA+ oesophageal/cardia 0.4 (0.2-0.8) CagA- Oesophageal/gastric cardia cancer 1.0 (0.5-1.7)	Age, sex, race, education and geographic center.	.
Vicari <i>et al</i> (1998) USA 1995-1997	21 patients undergoing endoscopy. Patients with known <i>H.pylori</i> status excluded; patients using antibiotics or bismuth-containing compounds within the last 30 days, prior gastric surgery, peptic ulcer disease, gastric cancer or dyspepsia excluded.	57 controls who underwent upper endoscopy for reasons other GERD. Potential controls taking proton pump inhibitors excluded as were those with known <i>H.pylori</i> status.	<i>H.pylori</i> and CagA status determined by histology and ELISA respectively.	<i>OD ratio</i> >1.0 for <i>H.pylori</i> whole cell. <i>OD ratio</i> >0.35 for $CagA^+$	Barrett's with dysplasia or carcinoma. <i>H.pylori</i> + 7 CagA+ 0	<i>H.pylori</i> + [0.60 (0.22-1.67)] <i>H.pylori</i> + CagA+ 0	None	RR not provided in paper; crude RR computed using data in paper.

Table 2.9. Case-control studies of *helicobacter pylori* infection and oesophageal adenocarcinoma

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
Grimley <i>et al</i> (1999) UK	40 cases undergoing oesophageal adenocarcinoma endoscopy in a single institution: >70% with mean ages of 74, 72, and 70 respectively.	46 patients undergoing endoscopy with normal mucosa. Male/female ratio=1 with mean age of 71.	Serology/ELISA anti <i>H.pylori</i> IgG (whole cell) CagA status by Western blot (116kDa antigen) VacA status by Western blot. Assay detects antibodies to at least 6 <i>H.pylori</i> antigens of molecular masses 19.5, 26.5, 30, 35, 89 and 116kDa.	<i>H.pylori</i> ⁻ <i>H.Pylori</i> + <i>CagA</i> ⁻ , <i>VacA</i> ⁻ <i>CagA</i> ⁺ , <i>VacA</i> ⁺ <i>CagA</i> ⁺ , <i>VacA</i> ⁻ <i>CagA</i> ⁺ , <i>VacA</i> ⁺	<i>H.pylori</i> + 24 <i>CagA</i> ⁺ 12 <i>VacA</i> ⁺ 5	<i>H.pylori</i> + [1.26 (0.54-2.95)] <i>CagA</i> ⁺ [0.67 (0.27-1.62)] <i>VacA</i> ⁺ [0.68 (0.21-2.18)]	None	Hospital based study RR not provided in paper; crude RR computed using data in paper.
Öberg <i>et al</i> (1999) USA	114 cases of oesophageal adenocarcinoma (includes tumours at gastroesophageal junction). 96 men, 18 women; median age 68 years. 37 cases had tumour of oesophageal and 77 of GEJ. RR limited to 37 oesophageal adenocarcinoma only.	229 patients with benign disease. 122 men, 107 women, median age 51 years, age range 16-85 years undergoing upper gastrointestinal endoscopy.	Histology Giemsa stain	<i>H.pylori</i> +	5	0.96(0.35-2.65)	Not reported	Hospital based study
Peek <i>et al</i> (1999)	30 cases of dysplasia/adenocarcinoma of the oesophagus.	48 controls drawn from consecutive patients undergoing endoscopy for reasons other than GERD symptoms or surveillance for Barrett's oesophagus. Controls had no symptoms or endoscopic signs of GERD.	Serology/ELISA Anti <i>H.pylori</i> IgG (whole cell) AntiCagA histology with Giemsa stain	<i>H.pylori</i> + <i>OD ratio</i> <i>1.0</i> <i>CagA</i> + <i>OD ratio</i> <i>>0.35</i>	<i>H.pylori</i> + 11 <i>CagA</i> + 3	0.81(0.32-2.07) 0.10(0.03-0.363)	None	

Table 2.9. Case-control studies of *helicobacter pylori* infection and oesophageal adenocarcinoma

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
Lord <i>et al</i> (2000) Australia 1990-1995	160 patients (123 male, 37 female, mean age 61.2 years) classified by highest grade of lesion in oesophagus: 35 adenocarcinomas, 5 Barrett's oesophagus with high grade dysplasia; 4 Barrett's oesophagus with high grade dysplasia; 28 Barrett's oesophagus with low grade dysplasia; 88 Barrett's intestinal dysplasia. Gastric antral biopsies available for 91(57%).	214 consecutive prospectively enrolled symptomatic patients (122 male, 92 female; mean age 57.2 years) who underwent upper GI endoscopy.	Modified Warthin-Starry silver staining in 5µm sections of formalin-fixed of paraffin embedded biopsy tissue from gastric antrum.	<i>H.pylori</i> +	8	[0.12 (0.05-0.25)]	No	RR not provided in paper; crude OR computed using available data.
Vieth <i>et al</i> (2000) Germany 1990-1997	297 patients with gastro-oesophageal reflux disease (GORD) including 138 patients with Barrett's mucosa and high grade dysplasia or carcinoma included in this analysis (age 65.0 ± 12.8, male:female ratio 4.9:1). Diagnosis determined by histologic examination of biopsies from upper GI tract.	712 patients with nonulcer dyspepsia (NUD). Mean age 40.1± 16.1 years; male:female ratio 0.3:1.	Gastric biopsies stained with Warthin-Starry silver stain for <i>H.pylori</i> .	<i>H.pylori</i>	NUD 468/712 Barrett's neoplasia 66/138 (47.8%)*	Ref p<0.01	NR	Insufficient data to compute RR.
					GORD 158/297	p<0.01		

Table 2.9. Case-control studies of *helicobacter pylori* infection and oesophageal adenocarcinoma

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
Weston <i>et al</i> (2000) USA 5-year period not specified.	289 patients undergoing oesophago-gastroduodenoscopy (EGD) at tertiary care hospital with histologically confirmed Barrett's: A minimum of 10 biopsies obtained at gastric surveillance. 20 cases with Barrett's with adenocarcinoma.	217 patients undergoing EGD for classic symptoms of GORD (heartburn or acid regurgitation at least weekly). Potential controls excluded if with presence of Barrett's oesophagus found; use of bismuth-containing compounds or antibiotics within previous 4 weeks; failure to obtain gastric surveillance biopsies or contraindication to performing biopsies; previous gastric or oesophageal resections or previous cure of <i>H.pylori</i> .	<i>H.pylori</i> colonization found in gastric biopsies stained with hematoxylin and eosin and use of a modified Giemsa and/or Steiner's silver stain of all biopsies.	<i>H.pylori</i> present if one or more biopsy specimens demonstrated typical <i>H.pylori</i> structures.	Barrett's adenocarcinoma 3	[0.22(0.07-0.73)]	No	Crude RR computed by the Working Group
El Omar <i>et al</i> (2003) USA	108 cases from a multicenter study in 3 geographic areas of USA.	Controls frequency matched to cases by 5-year age group and sex, selected by random digit dialing and Health Care Financing Administration roster sampling. 210 controls for <i>H.pylori</i> analysis; 224 controls for CagA analysis.	Serology/ELISA Anti- <i>H.pylori</i> antibodies	<i>H.pylori</i> + <i>CagA</i> +	35 5	<i>H.pylori</i> + 0.72(0.44-1.17) <i>CagA</i> + 0.33(0.12-0.87)	Age, sex, race (white, other)	Population-based study CagA Relative Risk represents CagA+ vs. <i>H.pylori</i> -. Study designed to evaluate risk associated with pro-inflamed cytokines gene polymorphism but none associated with AC or SCC.

Table 2.9. Case-control studies of *helicobacter pylori* infection and oesophageal adenocarcinoma

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
Wu <i>et al</i> (2003) USA 1992-1997	Cases with histologically confirmed adenocarcinoma aged 30-74 years, identified from population-based cancer registry for Los Angeles County were eligible. Number of cases: oesophageal adenocarcinoma, n=80; gastric cardia cancer, n=87; distal gastric cases, n=127. Oesophageal adenocarcinoma reported.	356 controls individually matched to cases on gender, race, and date of birth (± 5 years) selected from neighbourhood of residence of case. No history of gastric or oesophageal cancer.	Serology/ELISA anti <i>H.pylori</i> (whole cell) IgG anti CagA IgG on sera stored at -70°C	<i>H.pylori</i> seropositivity >1.0 plus borderline results (0.7-1.0)	49	Oesophageal adenocarcinoma Hp+ 1.01(0.58-1.77)	Age, gender, race, birthplace, education, smoking, body mass index	Population based cases and controls
				<i>CagA</i> seropositivity was mean ± 2 standard deviations from a series of known <i>CagA</i> negative serum samples by Western blot.	15	<i>CagA</i> +Hp+ 0.82(0.37-1.81)		
Ye <i>et al</i> (2004) Sweden	97 newly diagnosed patients with adenocarcinoma of the oesophagus (OA) and a 50% sample of patients with squamous cell carcinoma of the oesophagus (OSCC) (n=85). Cases restricted to <80 years of age; all tumours histologically confirmed and 97% of biopsy/surgical specimens reviewed.	820 controls randomly selected from Swedish Population Register and frequency matched to cases on age (by 10 year strata) and sex.	Serology/ELISA anti <i>H.pylori</i> IgG and anti <i>CagA</i> by immunoblot assay. Serum samples stored at -20°C and then further stored at -70°C.	<i>H.pylori</i> +.	18	0.3(2.0-0.6)	Age, sex, education, body mass index, smoking status, consumption of fruits and vegetables.	Population based design.
				<i>CagA</i> +	42	0.5(0.3-0.8)		

Table 2.9. Case-control studies of *helicobacter pylori* infection and oesophageal adenocarcinoma

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
Anandasabapathy <i>et al</i> (2007)	25 patients with a high grade dysplasia or oesophageal adenocarcinoma and <i>H.pylori</i> status in a larger study of incident and Barrett's Dysplasia diagnosed between January 2002 and September 2005. Cases were 94% male with a mean age of 59.23 years, 80% white.	30 controls with a diagnosis of intestinal metaplasia (Barrett's metaplasia) and <i>H.pylori</i> status data available.	Histology biopsy specimens stained with H&E, Giensa, or Diff-Quik	<i>H.pylori</i> +	4	0.38(0.10-1.41)	None	Control group with intestinal metaplasia (Barrett metaplasia) as an early stage lesion of outcome of interest (adenocarcinoma) would likely minimize case-control differences.
Derakhshan <i>et al</i> (2008) Iran	19 cases of histologically confirmed oesophageal adenocarcinoma.	38 age (\pm 4 years) matched controls selected from dyspeptic patients attending the same centre as cases and endoscopically determined to be free of peptic ulcer or tumour.	Serology/ELISA Anti- <i>H.pylori</i> IgG	<i>H. pylori</i> >30EIU (enzyme immune units)	9	0.32(0.10-1.02)	Smoking, GORD symptoms.	

Table 2.9. Case-control studies of *helicobacter pylori* infection and oesophageal adenocarcinoma

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
Anderson <i>et al</i> (2008) Ireland 2002-2005	Patients with histologically confirmed adenocarcinoma within the oesophagus. 131 oesophageal adenocarcinoma (OAC) cases	260 population controls.	Serology Western blot assay (Helicoblot 2.1)	<i>H.pylori</i> +	55	0.38(0.23-0.63)	Age, gender, occupation, year of education, body mass index, smoking and alcohol consumption location, parental occupation (manual, non-manual work) and household density in childhood.	Case-control study utilized data and samples in the FINBAR study.
				<i>CagA</i>	57	0.48(0.29-0.79)		
Früh <i>et al</i> (2008) USA and Canada	100 cases over 18 years of age, diagnosed within previous 6 months with histologically confirmed oesophageal adenocarcinoma. 88% male, mean age 64± 8 years, 100% Caucasian.	101 age and gender frequency matched controls were lifetime cancer-free, GERD-free, non-blood-related family members(usually spouses) and friends of other cancer/surgical patients. 87% male, mean age 36±8 years, 100% Caucasian.	Serology Helicoblot 2.1 (Genelabs)	<i>H.pylori</i> +	36	[0.76 (0.43-1.34)]	Adult BMI, Smoking status, age and gender	Hospital based study
				<i>CagA</i> ⁺	29	[0.97(0.53-1.77)]		