Table 1 Summary of responses to the question ''What is the most appropriate interval between colonoscopic surveillances in the following cases''

Clinical scenario	Most appropriate interval between colonoscopic surveillances					
	Surveillance not currently necessary	Annually	2 yearly	3 yearly	5 yearly	Other (please state)
37 y male. Left sided colitis of 18 y duration with concomitant PSC		**73.9 (56.0–91.8)**	17.4 (1.9–32.9)	8.7 (−2.8–20.2)		
44 y male. Proctitis rectum of 15 y duration with concomitant PSC	34.8 (15.3–54.2)	**47.8 (27.4–68.2)**	8.7 (−2.8–20.2)		4.3 (−4–12.6)	4.3 (−4–12.6)
73 y female. Extensive colitis of 45 y duration	4.3 (−4–12.6)	**47.8 (27.4–68.2)**	30.4 (11.6–49.2)	13.0 (−0.7–26.7)		4.3 (−4–12.6)
30 y male. Mild proctitis rectum of 9 y duration	**95.7 (87.4–104.0)**				4.3 (−4–12.6)	
45 y female. Crohn's colitis for 15 y	8.7 (−2.8–20.2)		34.8 (15.3–54.2)	**52.2 (31.8–72.6)**	4.3 (−4–12.6)	
50 y male. Left sided colitis of 22 y duration	39.1 (9.2–59.0)		17.4 (1.9–32.9)	**39.1 (9.2–59.0)**		4.3 (−4–12.6)
40 y female. Pancolitis of 11 y duration		4.3 (−4–12.6)	26.1 (8.15–44.0)	**69.6 (50.8–88.4)**		

Values are per cent respondents (95% confidence interval).
Answers corresponding to BSG guidelines are in bold type.
PSC, primary sclerosing cholangitis.

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Glucocorticoid receptor polymorphisms in inflammatory bowel disease

We read with interest the article by Mawdsley and Rampton on the relationship between psychological stress, increased disease activity in inflammatory bowel diseases (IBD), and the role of alterations in the hypothalamic-pituitary-adrenal (HPA) axis function (*Gut* 2005;**54**:1481–91). In IBD patients, chronic colonic inflammation induces downregulation of HPA axis responses, and animal studies have shown that altered function of the HPA axis renders rodents susceptible to stress induced increases in gastrointestinal inflammation. Central receptors located in the medial prefrontal cortex and hippocampus play a crucial role in glucocorticoid (GC) mediated counterregulation of stress induced HPA axis activation.[1]

Polymorphisms of the GC receptor (GR) gene may contribute to the large interindividual variations in sensitivity to GCs and HPA axis activity that are frequently observed in healthy individuals. Several polymorphisms of the GR gene have been described, and three of these are relatively frequent; however, knowledge of the influence of these polymorphisms on HPA axis response is very limited.

A genetic study was carried out in our laboratory to evaluate the incidence of these polymorphisms in 57 young patients with IBD (34 with Crohn's disease (CD) and 23 with ulcerative colitis (UC); mean age 13.8 years (range 1–45); 41.4% males, 58.6% females). The study was approved by the local ethics committee and written informed consent was obtained from all patients or their relatives or guardians. Studied polymorphisms have included *Bcl*I, in intron 2, and the N363S polymorphism in exon 2, that have been associated with an increased sensitivity to GCs in vivo,[2 3] and the ER22/23EK polymorphism, in exon 2, associated with a partial form of GC resistance.[4] Genomic DNA was extracted from peripheral leucocytes, amplified with specific primers, and subsequently digested with *Mnl*I (ER22/23EK), *Tsp*509I (N363S), or *Bcl*I restriction enzymes.[5 6]

The results of the analysis are presented in table 1. We found a significantly higher frequency of the *Bcl*I mutated genotype in patients with CD compared with healthy controls ($p = 0.03$, Fisher test; odds ratio 3.84 (95% confidence interval 1.23–11.91)). In contrast, no difference was observed between UC patients and controls.

The *Bcl*I polymorphism has been associated with high systolic pressure, insulin sensitivity, body mass index, and abdominal fat distribution[2 7]; carriers of the mutated allele have increased GC sensitivity and higher cortisol suppression after low dose dexamethasone.[8] A higher frequency of the mutated genotype was observed in this study in patients with CD; this mutation could lead to increased sensitivity in peripheral and central GRs, determining a raised susceptibility to feedback inhibition of GCs on the HPA axis. It is of interest that previous studies have demonstrated,[9] in a subgroup of patients with CD, alterations of the HPA axis resulting in relative hypocortisolism.

In contrast, no difference was observed for the N363S polymorphism, associated with increased sensitivity to GCs,[3 10] or for the ER22/23EK polymorphism, associated with a partial form of GC resistance (table 1).[4]

This is the first study to examine the possibility that IBD may be associated with GR polymorphisms; our results support the hypothesis that common polymorphisms in the GR gene may have modulating effects on the relation between psychological factors and HPA axis regulation in patients with CD. However, these data need to be confirmed in a larger group of patients.

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Table 1 *BclI*, ER22/23EK, and N363S genotype in patients with Crohn's disease (CD), ulcerative colitis (UC), and controls

	Genotype (n (%))			OR (95% CI)	
	Wild-type	Heterozygous	Mutated	Mutated *v* not mutated	p Value
BclI					
Controls (n = 70)	30 (42.9%)	34 (48.5%)	6 (8.6%)	–	–
CD (n = 34)	9 (26.5%)	16 (47%)	9 (26.5%)	3.84 (1.23–11.91)	0.03
UC (n = 23)	10 (43.5%)	12 (52.2%)	1 (4.3%)	1.03 (0.39–2.65)	1
ER22/23EK	Wild-type	Heterozygous	Mutated	Heterozygous *v* wild-type	
Controls (n = 70)	67 (95.7%)	3 (4.3%)	0 (0%)	–	–
CD (n = 34)	32 (94.1%)	2 (5.9%)	0 (0%)	1.39 (0.22–8.78)	0.6
UC (n = 23)	22 (95.7%)	1 (4.3%)	0 (0%)	1.01 (0.10–10.27)	1
N363S	Wild-type	Heterozygous	Mutated	Heterozygous *v* wild-type	
Controls (n = 70)	67 (95.7%)	3 (4.3%)	0 (0%)	–	–
CD (n = 34)	33 (97.1%)	1 (2.9%)	0 (0%)	0.68 (0.07–6.76)	1
UC (n = 23)	21 (91.3%)	2 (8.7%)	0 (0%)	2.13(0.33–13.60)	0.6

OR (95% CI), odds ratio (95% confidence interval).

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Effect of *Helicobacter pylori* eradication on precancerous lesions

We read with interest the paper by Mera and colleagues (*Gut* 2005;**54**:1536–40) on the effect of eradicating *Helicobacter pylori* infection on precancerous gastric lesions. However, we have concern regarding the extent to which the limited data provided in the paper support the authors' conclusions of regression of atrophy and intestinal metaplasia following *H pylori* eradication.

The main outcome reported was the average histological score. This is an arbitrary ordinal scale which is based on the presence of superficial gastritis, atrophic gastritis, intestinal metaplasia, dysplasia, or cancer as the most advanced lesion found in the four gastric biopsies performed at each time point. The average score was 3.77 at baseline, and following eradication of the infection decrease to 3.18 after 12 years. The extent to which resolution of the different components of the average histological score contributed to the fall in the score is not made clear in the paper. However, the authors do present data showing that the acute polymorphonuclear cell infiltration fully resolved and the chronic mononuclear cell infiltration partially resolved. The magnitude of the resolution of the inflammatory infiltrate would appear to be adequate to explain the fall in the average histological score without any associated resolution of the intestinal metaplasia or atrophy. The results section does not give information on the score for atrophy or intestinal metaplasia at baseline versus 12 years.

In the discussion section, comment is made to changes in atrophy and intestinal metaplasia. However, there are insufficient data to draw any meaningful conclusions or perform statistical analysis. In addition, there is clearly an error in the data provided is the discussion section as 70/182 is called 20%.

We would be grateful if the authors would provide individual metaplasia and atrophy scores at baseline and at 12 years in the two groups in order to allow independent analysis and interpretation of this important study. This is important as these are the lesions most strongly associated with cancer risk.

Our interpretation of the limited data made available in the current version of the paper is that there is evidence of early complete resolution of acute polymorphonuclear infiltration and partial resolution of chronic mononuclear cell infiltration but no convincing evidence presented of resolution of intestinal metaplasia or atrophy. The findings are therefore consistent with a number of previous studies showing no evidence of reversal of the important precancerous lesions. We also note that during the 12 years of follow up, five cancers occurred in the *H pylori* treatment group and four in the non-treatment group. Contrary to the conclusions of the authors, the benefit of eradicating *H pylori* infection in patients with advanced gastritis as a means of preventing cancer remains far from clear.

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Symptomatic gastro-oesophageal reflux in a patient with achlorhydria

Intraluminal impedance monitoring makes it possible to detect gastro-oesophageal reflux, independent of its pH.[1] This is useful because other factors apart from acidity are important in symptom generation.[2] Here, we describe a patient with achlorhydria in which impedance monitoring was used to identify gastro-oesophageal reflux as the cause of her symptoms.

A 72 year old female presented at our department. She complained of a retrosternal burning sensation which occurred at least five times a day. Eighteen months previously, her general practitioner prescribed monthly vitamin B12 injections after a routine blood test had revealed a megaloblastic macrocytic anaemia. She had underwent laparoscopic cholecystectomy for symptomatic gall stones four years previously.

Oesophageal manometry and 24 hour pH monitoring were performed. Results of oesophageal manometry were unremarkable. Ambulatory 24 hour pH monitoring showed an oesophageal acid exposure time of 0%; the lowest pH value that was reached was 5.5 (fig 1). Nine episodes of heartburn were reported by the patient but none was acid reflux related, resulting in a negative symptom index (SI) and symptom association probability (SAP) (both 0%).

After the results of pH monitoring had shown total absence of acid reflux, achlorhydria was suspected and further investigations were felt to be warranted. A blood test revealed normal values for blood cell counts and volumes and a slightly elevated serum vitamin B12 level (1080 pmol/l; normal 148–625). Serum gastrin was slightly high (135 ng/l; normal <75 for females). Tests for antibodies against parietal cells and intrinsic factor were positive. Upper endoscopy revealed an atrophic reddish mucosa of the gastric corpus and fundus. No oesophageal abnormalities were observed. Rapid urease tests were negative, indicating the absence of *Helicobacter pylori*. Microscopy revealed inflammation and intestinal metaplasia but no *H pylori*. A diagnosis of autoimmune atrophic gastritis was thus made. However, it was still unclear whether the patient's symptoms were the result of reflux of gastric contents.

Therefore, we decided to perform a 24 hour combined pH-impedance measurement. Again, pH data showed an acid exposure time of 0%, and no acid reflux episodes were measured. Analysis of the impedance signals showed 22 weakly acidic and five weakly alkaline reflux episodes. The patient experienced 11 episodes of heartburn, eight of which were preceded by a weakly acidic reflux episode, resulting in a positive SI and SAP for weakly acidic reflux (72.7% and 100.0%, respectively). The options of endoscopic or surgical antireflux treatments were considered but the patient responded well to intermittent sucralfate.

There is little information in the literature on reflux symptoms in patients with achlorhydria. Palmer described 22 cases of oesophagitis in patients with achlorhydria, also suggesting that non-acid reflux can induce oesophageal inflammation.[3] However, in Palmer's report, no mention was made of the symptoms experienced by his patients. Orlando and Bozymski described heartburn in