Methods: Thoraco-lumbar dorsal root ganglia were dissected from adult Wistar rats after CO₂ euthanasia and the sensory nerve cell bodies liberated using a collagenase and trypsin digest. Cells were incubated on poly lysine/laminin coated coverslips and incubated for 10–16 hours in nerve growth factor-supplemented neurobasal medium before being loaded with the calcium-sensitive ionophore FURA-2. The coverslips were transferred to a perfusion chamber mounted on an inverted fluorescence microscope. Cell activation was identified by spikes in intracellular calcium concentration using computerised image analysis. Cells were perfused with a pH 7.4 HEPES buffer before being exposed to pH 6.1 for 1 minute. After a further 10 minutes at pH 7.4 the perfusate was either continued or switched to an identical buffer containing 10⁻⁶M PGE₂ for 3 minutes prior to a second 1 minute exposure to pH 6.1.

Results: The number of cells imaged in each experiment was 19±3 (Mean±SEM). Thirty eight percent (±8%) of them responded to the first acid stimulus (n=10) with only 33±18% responding to the second stimulus (n=3). Addition of PGE₂ increased the proportion of cells responding to 45±8% (n=7), representing a rise of 40 ±17% versus a fall of 37±10% compared to respective baseline stimuli (p=0.03). Pre-incubation with indomethacin decreased viable cell count by a third but had no effect on the pH response of the surviving cells.

Conclusion: Exogenous PGE₂ increases the number of sensory nerve cells that respond to acid by reducing desensitisation and recruiting previously insensitive cells.

Symposium: the IBD service: 016–017

016 INFLAMMATORY BOWEL DISEASE IN THE COMMUNITY: DISEASE PROFILE, HEALTHCARE UTILIZATION, IMPACT ON LIFESTYLE AND PRODUCTIVITY

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Aim: To ascertain demographic and clinical characteristics, health-care utilisation and impact of disease on lifestyle/productivity in community patients with inflammatory bowel disease (IBD).

Methods: Anonymised structured questionnaires were mailed to all NACC members in the Bromley and Dartford area with IBD in March 2000. Data was collected on demography, type of IBD, duration of IBD and nature of specialist care. Annual frequency of consultations in primary/secondary care, hospitalisations for IBD, frequency of radiological/endoscopic investigations, surgical operation rates, use of medications/complimentary therapy was also ascertained. The impact of IBD on lifestyle/productivity was also determined.

Results: 107 out of 266 patients with IBD responded (40% response rate). Mean duration of NACC membership 6.1yrs. Sex (M:F) 38:69. Age n(%): <40yrs 39(36%), 40–70yrs 47(44%), >70yrs 18(17%). 14(13%) smoked regularly. 60(56%) had ulcerative colitis(UC), 44(41%) had Crohn's disease (CD). Mean duration of illness was 12.6yrs [UC vs CD; 9.8 vs 16.7, p=0.0056]. 84(79%) were under Gastroenterologist care and 24(22%) under surgical care. In addition 10(9%) were under other specialities for complications. *Use of healthcare resources:* In previous 12 months, mean frequency of visits to GP was 2.2, (range 0–16) and to hospital specialists 2.2, (range 0–14). Frequency of Abdominal radiology and colonoscopies over previous 5 years was mean(range) 1.7(0–29) and 1.3(0–7) respectively. Hospital admission rate over the past 12 months was 18/107(17%)[UC vs CD, 12% vs 25%, NS] and Lifetime surgical operation rate 33/107(31%)[UC vs CD, 8% vs 65 p<0.0001]. *Medications:* Patients took a mean of 6.8 tablets per day[UC vs CD, NS]. 32/83(38%) had been non-compliant in past one month. Patients were on the following medications n(%): 23(21%) on prednisolone[UC vs CD, NS], 6(6%) on budesonide, 87(81.3%) on 5ASA[UC vs CD, NS], 22(21%) on Azathioprine[UC vs CD, NS], 18(17%) on calcium tablets, 13(12%) on acid suppressants. Only 7/23(31%) of patients on prednisolone were on calcium tablets. 6/22(27%) of patients on azathioprine were on prednisolone as well. 28/107(26%) had used complimentary therapy for IBD. *Effect on lifestyle:* 83(77%) patients with IBD over the previous one month had no or minimal limitation of lifestyle. In the previous 6 months, the mean days lost off work was 5.1 (range 0–99)[UC vs CD, NS].

Conclusion: IBD patients in the community place substantial pressures on healthcare but majority enjoy relatively good health with few limitations on employment and lifestyle.

017 AN ANALYSIS OF THE HOSPITAL COSTS OF INFLAMMATORY BOWEL DISEASE IN UK

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The economic burden of inflammatory bowel disease (IBD) on society and health care systems is high due their occurrence during the economically productive years and chronic nature. Published literature on the economics of IBD are however limited and this has relevance with the introduction of new expensive treatments such as anti-TNF antibody.

Aim: To examine the total hospital costs of IBD patients over a year.

Methods: 100 consecutive IBD patients attending our multidisciplinary clinic were studied. Patient records were studied to collect data on the number of outpatient attendances, inpatient hospital days, cost of laboratory, radiological, endoscopic investigations and treatment costs incurred per patient over a 12-month period.

Results: 62 patients with ulcerative colitis and 38 with Crohns disease were studied. There were 44 male and 56 female patients. The mean age for both sexes combined were 47.8yrs (18–79) for UC and 46.5yrs (21–84) for Crohns. The median disease duration was 126.5 months (13–456) and 174 months (16–456) for UC and Crohns respectively. The mean total costs per patient per year for UC was £1096 (95%CI 855–1337) and £2184 (95%CI 1433–2935) for Crohns respectively. As the data was skewed the calculated median charges were lower than the mean, £903 (80–4644) for UC and £1276 (98–9534) for Crohns. The following table illustrates costs for UC and Crohns represented as mean with 95% CI intervals.

Abstract 17, Table 1

Costs	UC	Crohns
Inpatient (incl. Surgery)	£1755 (1297–2213)	£2738 (1802–3674)
Outpatient	£210 (176–244)	£267 (209–325)
Investigation	£258 (170–346)	£338 (210–466)
Medications	£487 (384–590)	£642 (478–806)

The percentage of total costs for ulcerative colitis and Crohns disease are as follows, Inpatient 13% & 43%, Outpatient 19.1% & 12.2%, Investigations 23.5% & 15.4% and Medications 44.4% & 29.4%.

Conclusion: The hospital costs of IBD patients are high. This is particularly relevant with the availability of newer treatments, which are expensive but could reduce the inpatient hospital days and avoid surgery and thus prove to be cost effective.

327 DOES BETTER DISEASE RELATED EDUCATION IMPROVE QUALITY OF LIFE? A SURVEY OF IBD PATIENTS

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Background and aims: The importance of Health Related Quality of Life (HRQOL) assessment in patients with chronic disorders such as inflammatory bowel disease (IBD) is now acknowledged by researchers. Of the many factors which may influence HRQOL, patient knowledge of the condition and disease related information provision have hitherto not been studied.

Patients and methods: 250 patients with inactive IBD (UC=122, CD=128) were randomly chosen from our IBD clinic. Two sets of questionnaires (initially a standard questionnaire to assess level of disease related information (PIS), followed by a HRQOL questionnaire) were sent to each patient. In the PIS a score of 7 or more indicated satisfactory disease related knowledge and in the HRQOL a scores less than 51 suggested a normal QOL, and a score above 60 significantly impaired QOL.

Results: 168 patients (66%) returned both the questionnaires (UC=91, CD=77). The mean QOL in patients with UC and CD was 62.2 ± 8.3 and 63.9 ± 9.5 respectively, (p=ns). 99 patients (59%) had significantly impaired QOL (mean score 65 ± 7.6) with only 12

patients (8%), 6 in each group, having a normal QOL. Mean PIS score for the patients was 7.04 ± 0.1 . 53% of the UC patients and 75% of the CD patients ($p=0.006$) were considered well informed (ie. PIQ scores of 7 or more). The mean PIS for UC patients was 6.5 ± 0.4 vs 7.5 ± 0.2 for the CD group ($p=0.001$). There was however no correlation seen between the QOL and PIS scores, both for UC and CD patients ($r=0.3$).

Conclusion: Most patients with IBD have impaired QOL, inspite of having inactive disease. The level of disease related knowledge appears to be better in patients with CD, though that does not seem to affect QOL.

H. pylori/Upper GI/Oesophagus Free Papers: 018-032

018 *HELICOBACTER PYLORI* INFECTION REDUCES SYSTEMIC AVAILABILITY OF DIETARY VITAMIN C

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H. pylori infection is recognized to lower the concentration of vitamin C in gastric juice. The objective of this study was to assess whether this effect of the infection on intragastric vitamin C resulted in reduced bioavailability of the ingested vitamin.

Methods: The study involved 1106 men and women aged 25-74 randomly recruited from the population of north Glasgow. Their *H. pylori* status was determined by measuring serum IgG antibody titres to *H. pylori* using a validated ELISA (Bio-Rad Laboratories Ltd., England). Dietary vitamin C intake was calculated from a food frequency questionnaire. Plasma vitamin C concentrations were measured by a fluorometric assay. Correction was made for potential confounding factors such as age, sex, smoking and social status.

Results: Sixty three percent were *H. pylori* seropositive. The mean plasma vitamin C concentration in those who were *H. pylori* positive was only 65% of that in those classified negative ($p<0.0001$). This was partly explained by the fact that the dietary intake of vitamin C of the *H. pylori* positives was only 86.5% of that of the negatives ($p<0.0001$). Correction for the reduced dietary intake and other potential confounding factors included age, sex, social class and smoking still gave a plasma vitamin C level for *H. pylori* positives which was only 80% of that for the *H. pylori* negatives ($p<0.0001$).

Conclusions: *H. pylori* substantially impairs bio-availability of vitamin C. This, together with the reduced vitamin C intake of *H. pylori* positive subjects markedly reduces the plasma vitamin C level of infected subjects. The reduced circulating levels of vitamin C in *H. pylori* infected subjects may contribute to the aetiology of gastric cancer, as well as other diseases associated with antioxidant deficiency.

019 ADAM17 AND TIMP3 mRNA EXPRESSION IN GASTRIC MUCOSA INFECTED WITH *H. PYLORI* AND IN GASTRIC CANCER

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Introduction: ADAM17 (a disintegrin and metalloproteinase) protein is implicated in the shedding of TNF α , TGF α , L-selectin and the p75 TNF receptor. Our previous work demonstrated that *H. pylori* induced ADAM17 gene expression in gastric epithelial cells.

Aims: To examine ADAM17 and the specific inhibitor TIMP3 mRNA expression in gastric mucosa of patients infected with *H. pylori* and patients with gastric cancer.

Methods: Endoscopic antral and corpus biopsies were obtained from 54 dyspeptic patients without any medication and 9 gastric cancer operative sections for semiquantitative PCR and histology. The ratio of ADAM17 and TIMP3 transcripts to that of G3PDH was determined by computer image analysis.

Results: In the antral mucosa, ADAM17 mRNA expression in patients with *H. pylori* infection (mean $\pm$ SEM 0.24 ± 0.07 , $n=27$) was significantly greater ($p<0.05$) than in uninfected patients with normal mucosa (0.08 ± 0.04 , $n=16$). There was a significant correlation ($p<0.05$) between the expression of ADAM17 and mononuclear cell infiltration. ADAM17 transcripts in gastric cancer mucosa (0.40 ± 0.10 , $n=9$) were also upregulated ($p<0.01$) compared with normal mucosa. TIMP3 mRNA expression was greater in gastric cancer mucosa (1.0 ± 0.11 , $n=7$) than in normal mucosa (0.41 ± 0.12 , $n=11$, $p<0.01$) and *H. pylori* infected mucosa (0.65 ± 0.11 , $n=9$, $p<0.05$).

Conclusion: ADAM17 mRNA expression was increased in *H. pylori* infected mucosa and in patients with gastric cancer. ADAM17 is likely to be important in the inflammation induced by *H. pylori* and may also be relevant to the development of malignancy. TIMP3 mRNA expression was also upregulated in gastric cancer mucosa. Further studies are required to localise the cellular origin of ADAM17 and TIMP3 in normal gastric mucosa and in gastric cancer.

020 *HELICOBACTER PYLORI* LEADS TO DECREASED SURFACE EXPRESSION OF β -CATENIN IN EPITHELIAL CELLS

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Background: *H. pylori* is implicated in the pathogenesis of gastric cancer. The cadherin-catenin complex (of which β -catenin is a key signalling component) promotes stable adhesion of epithelial monolayers and is altered in several epithelial cancers, including gastric cancer. Furthermore, germline mutations in the E-cadherin gene have been described in familial gastric cancer.

Aim: To assess the effect of *H. pylori* on cadherin-catenin expression in the HT29 epithelial cell line.

Methods: *H. pylori* strain 60190 (*vacA* s1/m1, *cagA*+) was cocultured with HT29 cells for 24 hours at 37°C. Cells were also incubated with VacA (purified from 60190 by broth culture, precipitation, anion exchange and gel filtration chromatography). Using monoclonal antibodies and confocal microscopy, the distribution of E-Cadherin and β -catenin was studied in two consecutive optical slices, taken 5 μ m apart. Intensity of staining was graded as strong/weak/absent in 200 cell-cell junctions (systematic random selection) from treated and control cells. Immunoblotting was performed for α , β , γ -catenin and E-Cadherin on lysed cell extracts. Experiments were performed on three occasions.

Results: HT29 cells possessed the entire cadherin-catenin complex; the adhesion molecules were localised to junctional membrane domains. Co-culture with *H. pylori* (1000 bacteria/cell) lead to a consistent decrease in surface expression of β -catenin (typical experiment: strong staining in 89% of cell-cell junctions in untreated cells vs. 35% in *H. pylori*-exposed cells). No redistribution of β -catenin to nuclear regions was noted. Intensity and localisation of E-cadherin remained unchanged. No gross changes were seen with VacA addition. Immunoblots confirmed expression of E-cadherin and the three catenins and no gross alterations were seen with *H. pylori* co-culture.

Conclusion: Co-culture of *H. pylori* with epithelial cells leads to perturbation of β -catenin but has no effect on E-cadherin. Modification of β -catenin may be important in the pathogenicity of *H. pylori*.

021 "TWO WEEK WAIT" GUIDELINES FOR UPPER GASTROINTESTINAL CANCER - DO THEY WORK?

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Introduction: National guidelines have recently been introduced with the aim of facilitating the earlier diagnosis and treatment of cancer. In the case of upper GI cancer, there is little published evidence to support the use of these guidelines.

Methods: We performed a prospective audit of all referrals for upper GI cancer under the two week wait guidelines, during the first 2 months the system was in operation at a single teaching hospital. We collected demographic data, clinical details and final diagnoses on all patients. We also collected the same data on all patients who had an upper GI cancer diagnosed during the same period who were not referred by the "2 week wait".