constipation but their relative clinical performance is unclear. Our aim was to investigate the diagnostic yield and clinical outcomes of DFP and ARM in chronic constipation.

Methods Patients who had undergone both DFP and ARM over a 3-year period were studied retrospectively. Demographics, treatment and clinical outcomes were recorded. The diagnosis was recorded as "mixed" if investigation showed evidence of both anismus and anatomical problems such as rectocoele, intussusception or prolapse. The clinical outcome was defined as positive if the test resulted in treatment with symptomatic improvement, or resolution at follow-up. To determine whether there was a selection bias in those undergoing both DFP and ARM we additionally looked at the two groups having solely DFP or ARM from the same period.

Results DFP and ARM group: 43 patients (40 female, 58% surgical referrals; age range 17–85 years; median 46) underwent both DFP and ARM. The diagnostic yield for DFP was higher at 98% (anismus 44%, anatomical 40%, mixed 14%; normal 2%) vs 47% for ARM (anismus 26%, mixed 21%; normal 53%). There was diagnostic concordance in only 11 (26%), partial concordance in 9 (21%) and discordance in 23 (53%) patients. Although the diagnostic yield of DFP was much greater than ARM in this combined group, both tests led to similar positive outcomes regardless (47% in DFP vs 45% in ARM) when tests revealed a pathology. Single investigation groups: 10 patients had DFP alone (8 female, 60% surgical referrals; age range 22–73 years, median 55) with a diagnostic yield of 90% (anismus 30%, anatomical 50%, mixed 10%; normal 10%). The positive outcome in those with a detectable pathology was 33%. 15 patients had ARM alone (14 female, 27% surgical referrals; age range 19–75 years, median 50) with a diagnostic yield of 67% (anismus; 33% normal). The positive outcome in those with a detectable pathology was 70%.

Conclusion DFP had a higher diagnostic yield than ARM, but concordance was poor. Greater diagnostic yield did not translate into more positive clinical outcomes either. The clinical impact of additional DFP-based diagnoses is therefore questionable. The single test cohort data suggest that patients having DFP alone are a different clinical population from those who accessed both tests, since diagnostic yields and clinical outcomes were higher for ARM alone. The latter group were predominantly medical gastroenterology referrals. Further study is required to design optimal investigation strategies for chronic constipation.

Competing interests None declared.

PWE-007 PARACRINE PROSTAGLANDIN-E SIGNALLING MODULATES CANINE GASTRIC EPITHELIAL CELL MIGRATION

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Introduction Gastric ulceration is a limiting complication of therapy with cyclooxygenase (COX) antagonists, widely used anti-inflammatory/analgesic drugs in both humans and dogs. COX-derived prostaglandin E (PGE) has an important role in gastric defense and cytoprotection via promotion of blood flow and mucus secretion and inhibition of gastric acid secretion. Given the importance of gastric epithelial cell migration in reestablishing epithelial integrity following gastric damage, we have investigated whether paracrine PGE signalling has a role in the modulation of gastric epithelial cell migration.

Methods In order to retain paracrine signalling between different cell types, we isolated intact gastric glands via collagenase digestion of canine gastric mucosal tissue. Isolated glands spread in vitro to form islands of cells. The rate of gland spreading over 48h was measured as a surrogate for cell migration speed. Lamellipodia protrusion was analysed as an index of spreading activity. A value for lamellopodia area was calculated by measuring spread area minus area bounded by nuclei of cells at the edge of spread glands. Spread glands, when serum-starved, exhibit a reduction in area. We added both a selective and a non-selective COX antagonist and PGE_2 to serum-starved glands to assess their effects on migration. All treatments were added blindly to eliminate bias. Statistical significance was assessed using univariate analysis of variance. Expression of COX-2 and PGE receptors (EP-3 and EP-4) was assessed by RT-PCR and immunohistochemistry.

Results RT-PCR confirmed COX-2, EP-3 and EP-4 expression in our samples. COX-2 immunoreactivity was present in the majority of gland cells. The COX 1/2 antagonist indomethacin (50 μM) decreased spreading (0.85-fold, $p<0.05$, $n=5–9$ for all experiments) and lamellipodia area (0.3-fold, $p<0.05$). The COX-2 selective antagonist NS-398 (10μM) caused similar decreases to indomethacin (0.8-fold and 0.65-fold respectively, $p<0.05$). PGE (1μM) prevented a 0.7-fold reduction in island area elicited by incubation in serum free medium ($p<0.05$).

Conclusion This data shows a role for COX-2 derived PGE in the promotion of gastric cell migration and cellular lamellipodia formation. A reduction of mucosal PGE via COX-2 antagonism may therefore inhibit gastric epithelial cell migration contributing to COX-antagonist elicited gastric ulceration in both humans and dogs.

Competing interests None declared.

Oesophageal II

PWE-008 DO STATINS PREVENT THE HISTOLOGICAL SUBTYPES OF OESOPHAGEAL CANCER? PROSPECTIVE DATA FROM THE UK GENERAL PRACTICE RESEARCH DATABASE (GPRD)

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Introduction The incidence of oesophageal adenocarcinoma (OAC) has risen dramatically in the Western world and is associated with a poor prognosis. Statins show anti-cancer properties in experimental work with OAC cell lines for example reduced cell proliferation, increased apoptosis. This study aimed to investigate if statins are negatively associated with the development of two different histological subtypes of oesophageal cancer, OAC and oesophageal squamous cell cancer (OSCC), in a prospective cohort study.

Methods The cohort was over 4 million people in the General Practice Research Database (GPRD), a UK database of 488 nation-wide general practices. Information is recorded on medication use prior to development of other illnesses, including cancers. Statin use was defined as a prescription for a minimum of 10 months preceding diagnosis of oesophageal cancer. Approximately half the GP practices in the GPRD are linked to the NHS cancer registry, allowing identification and sub-classification of histologically confirmed cases of OAC and OSCC. Each case was matched with four controls and conditional logistic regression estimated the OR plus 95% CIs for the development of each type of cancer, adjusted for diabetes, BMI, smoking, aspirin, PPIs and drugs that relax the lower oesophageal sphincter.

Results 581 histologically confirmed cases of OAC (77.8% men, mean age 70.7 years, SD=11.4) and 332 cases of OSCC (38.6% men,