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TITLE PAGE

Title: Minimal Differences in Prevalence and Spectrum of Organic Disease at Upper Gastrointestinal Endoscopy Between Selected Secondary Care Patients with Symptoms of Gastro-oesophageal Reflux or Dyspepsia.

Short title: Organic Disease in Gastro-oesophageal Reflux and Dyspepsia.

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Abbreviations:

ANOVA	analysis of variance
BMI	body mass index
GI	gastrointestinal

SD standard deviation

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ABSTRACT

Objectives: Gastro-oesophageal reflux and dyspepsia are common upper gastrointestinal (GI) conditions, which are felt to be separate entities. We aimed to measure the degree of overlap between the two, and assess whether endoscopic findings differed between them.

Material and Methods: Complete demographic, symptom, upper gastrointestinal (GI) endoscopy, and histology data were collected from consecutive adult patients in secondary care. Patients were categorised according to whether they reported gastro-oesophageal reflux alone, dyspepsia alone, or both, and patient demographics and endoscopic findings were compared between these three groups.

Results: Full data were collected for 1167 selected patients, of whom 97 (8.3%) had gastro-oesophageal reflux only, 571 (48.9%) had dyspepsia alone, and 499 (42.8%) had overlapping symptoms. Patients with overlap symptoms were more likely to be smokers, compared with those with gastro-oesophageal reflux only, or dyspepsia alone (P=0.009), but there were no other differences. Patients with gastro-oesophageal reflux only or overlap had a significantly higher prevalence of erosive oesophagitis (18.6% and 15.4% respectively, $P < 0.001$), but this was still the commonest diagnosis among those with dyspepsia alone (7.2%). No significant differences were seen in prevalence of other endoscopic findings.

Conclusions: Gastro-oesophageal reflux and dyspepsia symptoms commonly overlap. There were minimal differences in either patient demographics or the spectrum of underlying organic disease between the various symptom groups, suggesting that restrictive classifications according to predominant symptom may not be clinically useful.

Keywords: epigastric pain; heartburn; regurgitation; endoscopy

Introduction

Dyspepsia and gastro-oesophageal reflux are common complaints in the community. [1, 2, 3] Although there has been controversy about the symptoms that make up the constellation of dyspepsia, over the last 30 years definitions have moved away from one that consists of any symptom referable to the upper gastrointestinal (GI) tract, [4] towards a more restrictive classification system encompassing upper abdominal pain or burning, early satiety, or post-prandial fullness. [5, 6] The aetiology of dyspepsia is varied, with the majority of cases functional in origin, and the remainder secondary to a range of organic pathology, such as peptic ulcer disease or gastric cancer. [7] Gastro-oesophageal reflux relates to the sensation of retrosternal burning, discomfort, or pain, [8] and can be caused by retrograde movement of acidic stomach contents into the lower oesophagus, leading to erosive or non-erosive reflux disease, or it too may be functional in origin, due to oesophageal hypersensitivity.

As definitions of the symptom groups of dyspepsia and gastro-oesophageal reflux have evolved, they have become mutually exclusive. However, previous studies have shown there is considerable overlap between symptoms of gastro-oesophageal reflux and dyspepsia. In a community-based survey, 56% of dyspeptic patients also had gastro-oesophageal reflux, and 63% of patients with gastro-oesophageal reflux also had dyspepsia. [9] Among 300 patients in primary care who presented with upper GI symptoms, over half of patients meeting criteria for functional dyspepsia also reported gastro-oesophageal reflux. [10] In another study assessing 200 patients with suspected non-erosive reflux disease, those with normal pH monitoring, and therefore likely to have functional heartburn, were significantly more likely to report symptoms compatible with functional dyspepsia, such as early satiety and post-prandial fullness, than those with confirmed non-erosive reflux disease. [11]

Between 60% and 80% of patients with dyspepsia will have a normal upper GI endoscopy, [7, 12, 13] so most dyspepsia management guidelines advocate empirical medical therapy, with upper GI endoscopy reserved for particular patient groups, for example those with alarm symptoms, or over the age of 50 to 55 years. [14, 15, 16] In contrast, gastro-oesophageal reflux is usually thought to be indicative of underlying erosive oesophagitis, and may be a risk factor for Barrett's oesophagus and oesophageal adenocarcinoma. [17, 18] This has led to the suggestion, by some, that patients undergo upper GI endoscopy to screen for these conditions. [19] However, with the ever evolving classification of dyspepsia and gastro-oesophageal reflux, and the potential for symptom overlap, it may be difficult to separate these two groups of patients, particularly in the community or primary care. [20] Such an approach may therefore be futile. We postulated that patients with dyspepsia and gastro-oesophageal reflux would exhibit large degrees of symptom overlap, even in secondary care, and also that symptoms would not predict endoscopic findings.

Materials and Methods

Participants and Setting

The study was conducted in two gastroenterology referral centres in Hamilton, Ontario serving a local population of 520,000 individuals. All patients were referred from primary care for assessment of GI symptoms. Consecutive potentially eligible adults aged ≥16 years were approached at McMaster University Medical Center and St. Joseph's Healthcare, before consulting with the gastroenterologist, and were provided with a patient information leaflet outlining the study. The only exclusion to participation was the inability to understand written English. Written informed consent was gathered from all recruited subjects. Ethical approval was granted in January 2008 by the Hamilton Health Sciences and McMaster University research ethics board, at which point recruitment commenced, finishing in December 2012. This dataset has previously been used to publish studies examining the utility of symptoms in predicting a diagnosis of irritable bowel syndrome, functional dyspepsia, and inflammatory bowel disease, as well as characteristics of patients with functional GI disorders. [12, 21, 22, 23, 24, 25, 26, 27] There is no overlap between the data reported in this study and previous studies.

Data Collection and Synthesis

Demographic and Symptom Data

At the initial clinic visit basic demographic and symptom data were collected. Demographic data included age, sex, educational level, marital status, ethnicity, alcohol and tobacco use, height (in metres), and weight (in kilograms) which were then used to calculate

body mass index (BMI). The Rome III diagnostic questionnaire for functional GI disorders was used to record symptom data. This is a 93-item instrument, which takes approximately 20 minutes to complete, and has been validated previously. [28] Collected data were inputted into a database by a trained researcher who was not involved in the clinical care of patients, thereby ensuring assessors were blinded to the symptom status of participants.

Definitions of Gastro-oesophageal Reflux Symptoms, Dyspepsia, and Overlap

We used the symptom items of heartburn, epigastric pain, early satiety, or postprandial fullness within the last 3 months from the Rome III questionnaire to define the presence of gastro-oesophageal reflux symptoms or dyspepsia. Patients were classified as having gastro-oesophageal reflux symptoms if they reported heartburn (a burning discomfort or pain behind your breastbone) at a frequency of once a week or more. Those who reported early satiety, postprandial fullness, or epigastric pain (pain or burning in the middle of your abdomen above your belly button, but not in your chest) at a frequency of once a week or more were classified as having dyspepsia. It should be noted that this definition of dyspepsia is not compatible with the Rome III criteria for functional dyspepsia, [6] which require a minimum symptom duration, and also include no evidence of structural disease at upper GI endoscopy that would explain the symptoms.

Patients were then classified as having gastro-oesophageal reflux symptoms only, dyspepsia only, or overlap of gastro-oesophageal reflux symptoms with dyspepsia. We further subdivided patients with overlap of gastro-oesophageal reflux symptoms and dyspepsia according to the predominant syndrome present, using symptom frequency. For instance if a patient reported heartburn at a frequency of once a week, but epigastric pain, early satiety, or postprandial fullness at a frequency of every day, they were classified as

dyspepsia-predominant. Patients reporting heartburn at a frequency of every day, but epigastric pain, early satiety, and postprandial fullness at a frequency of once a week, were classified as gastro-oesophageal reflux-predominant. Finally, patients who reported identical symptom frequencies for both heartburn and symptoms of dyspepsia were classified as overlap with no symptom predominance.

Endoscopic and Histopathologic Data

All patients underwent an upper GI endoscopy to the second part of the duodenum, using a Pentax endoscope (Pentax Canada, Inc) following a 6 hour fast. Endoscopists were blinded to the questionnaire data of patients. Endoscopic findings were recorded on the endoPRO reporting system (Pentax Canada, Inc, Mississauga, Ontario, Canada), which was accessed in order to collect data on ultimate endoscopic diagnosis. The following were classed as organic findings at upper GI endoscopy: erosive oesophagitis, Barrett's oesophagus, benign oesophageal stricture, Schatzki ring, oesophageal carcinoma, oesophageal candidiasis, eosinophilic oesophagitis, gastric ulcer, gastric cancer, duodenal ulcer, coeliac disease, and upper GI Crohn's disease. Cystic fundic gland polyps, gastritis diagnosed after histological interpretation of gastric biopsy specimens, or duodenitis, defined as erythema in the duodenum seen at upper GI endoscopy, were not considered as organic disease.

Biopsy specimens were taken if the endoscopist felt they were clinically indicated at the time of upper GI endoscopy. All biopsy specimens were reviewed by experienced histopathologists, who were also blind to questionnaire data, with findings recorded using the MEDITECH Healthcare Reporting System (Medical Information Technology, Inc, Westwood, MA). Investigators accessed this system to retrieve data on histopathologic

diagnosis. Organic disease after histopathological interpretation of biopsy specimens included: Barrett's oesophagus, reflux or eosinophilic oesophagitis, oesophageal squamous cell carcinoma or adenocarcinoma, oesophageal candidiasis, gastric adenocarcinoma, gastric carcinoid, upper GI Crohn's disease, coeliac disease, villous atrophy due to other causes, or duodenal adenocarcinoma.

Statistical Analysis

To assess for differences in demographic characteristics between groups, continuous variables were expressed as means and standard deviations (SD), and compared using a one-way analysis of variance (ANOVA). Categorical demographic variables, and prevalence of organic findings at upper GI endoscopy, were compared between groups using a χ^2 test, or Fisher's exact test when cell numbers were small. We also compared demographic characteristics and symptoms between those undergoing upper GI endoscopy and those who did not, using a χ^2 test for categorical data, and an independent samples t-test for continuous data, with a mean and standard deviation (SD), in order to assess whether those who underwent upper GI endoscopy were representative of all patients seen in the two GI outpatient clinics. Due to multiple comparisons, statistical significance was defined as a P value of <0.01 for all these analyses, which were performed using SPSS for Windows version 21.0 (SPSS Inc, Chicago, IL, USA).

Results

A total of 5978 patients attended the two outpatient clinics during the study period, with 4224 (70.7%) giving informed consent to take part. In total, 1605 (38.0%) of these 4224 patients underwent complete endoscopic evaluation for their upper GI symptoms. However, 285 (17.8%) of these 1605 patients did not report heartburn or dyspepsia as the indication for upper GI endoscopy, and a further 153 (9.5%) patients had incomplete data, meaning that 1167 (72.7%) individuals (mean age 47.3 years (range 16 to 91 years), 781 (66.9%) female) provided complete data for these analyses (Figure 1). There were few differences in demographic characteristics between the 1605 patients undergoing upper GI endoscopy, and the remaining 2619 patients who did not. Those who underwent endoscopy were significantly older, more likely to drink alcohol, and were less likely to be White Caucasian, but in all instances the absolute magnitude of these differences was small (Supplementary Table 1). As would be expected, the proportion of individuals reporting the upper GI symptoms of interest was markedly higher among those undergoing endoscopy.

There were 97 (8.3%) participants with gastro-oesophageal reflux symptoms only, 571 (48.9%) with dyspepsia only, and 499 (42.8%) with overlap of gastro-oesophageal reflux symptoms and dyspepsia (Figure 2). Of the 496 patients with overlap who provided sufficient symptom data to allow predominant symptom to be examined, 41 (8.3%) were gastro-oesophageal reflux-predominant, 148 (29.8%) had dyspepsia as the predominant symptom, and the remaining 307 (61.9%) reported no predominant symptom.

Supplementary Table 2 shows demographic data for participants according to symptom group. There were no significant differences between groups for age, gender, alcohol use, marital status, educational level, or ethnicity. There was a trend towards a lower BMI in those with dyspepsia only, and participants in the overlap group had significantly

higher rates of tobacco use. Demographic data for the group with overlap symptoms, according to predominant symptom, are provided in Supplementary Table 3. No significant differences were seen between these groups.

Endoscopic Findings

Overall, prevalence of any organic disease was generally higher in the gastro-oesophageal reflux symptoms only group (32.0%) than either the dyspepsia alone group (21.7%), or those with overlap (26.9%), but this was not statistically significant (P = 0.035). Within the overlap group there was no significant difference in the prevalence of any organic disease between predominant symptom groups (31.7% gastro-oesophageal reflux-predominant, 23.0% dyspepsia-predominant, 28.0% overlap with no symptom predominance, P = 0.40).

Table 1 shows the prevalence of organic disease in those with gastro-oesophageal reflux symptoms only, dyspepsia only, and overlap of symptoms. There were no significant differences in the prevalence of any endoscopic findings between groups, other than a significantly higher prevalence of erosive oesophagitis (18.6%) in the gastro-oesophageal reflux symptoms only group, compared with the dyspepsia only (7.2%), and overlap (15.4%) groups (P < 0.001). Despite this, erosive oesophagitis was the commonest organic finding in all three groups. Organic findings for the group with overlap of gastro-oesophageal reflux and dyspepsia symptoms, according to predominant symptom, can be seen in Table 2. There were no significant differences in prevalence of organic disease between groups.

Discussion

This study compared demographic features and endoscopic findings between selected patients presenting with symptoms of dyspepsia and gastro-oesophageal reflux, and examined the degree of overlap between them. It demonstrated that symptoms of heartburn, epigastric pain, and post-prandial distress perform poorly in predicting erosive oesophagitis and peptic ulcer disease. There were minimal differences in both patient characteristics and prevalence and spectrum of underlying organic pathology between those with dyspepsia, those with gastro-oesophageal reflux, and those with overlap between the two. The only significant difference in demographic features found was that those with overlap of gastro-oesophageal reflux and dyspepsia were more likely to smoke tobacco. The prevalence of individual organic diseases was similarly distributed, with the exception of erosive oesophagitis, which was significantly commoner among patients presenting with gastro-oesophageal reflux or overlap. However, this was still the commonest organic finding at upper GI endoscopy in the other two groups of patients. Finally, there was overlap between gastro-oesophageal reflux symptoms and dyspepsia in more than 40% of individuals.

Strengths of this study include the large sample size of over 1100 patients. Recruitment took place in a secondary care setting so the results are likely to be representative of other secondary care populations, although care should be taken when extrapolating the findings to primary care. However, organic findings at upper GI endoscopy are likely to be even rarer among patients with upper GI symptoms in the latter setting. Our results therefore suggest that using symptoms to predict underlying organic pathology in primary care is likely to be an approach fraught with even greater uncertainty. Validated questionnaires including the Rome III diagnostic questionnaire were used for data collection. [28] As such, the definitions used for dyspepsia and gastro-oesophageal reflux symptoms mirror current agreed definitions of these conditions closely. [5, 8]

Weaknesses of this study include the fact that it was conducted in a referral population. Individuals in the community who experienced upper GI symptoms self-selected as to whether or not to consult in primary care, and the responsible primary care physician then made a judgement as to whether there were features that warranted referral on to secondary care. In addition, once assessed in secondary care, not all patients presenting with gastro-oesophageal reflux, dyspepsia, or overlap were required to undergo upper GI endoscopy as part of their assessment. Upper GI endoscopy was performed only when deemed clinically indicated by the assessing gastroenterologist. In total, >70% of all patients approached gave informed consent to participate, and of these >25% provided complete symptom data and underwent upper GI endoscopy. As some patients with gastro-oesophageal reflux symptoms and/or dyspepsia did not undergo endoscopy, without endoscopic and histopathologic data on these subjects, it is impossible to say how these participants may have affected the observed results if they were included. The precise reasons why some patients were not subject to upper GI endoscopy cannot be elucidated from this study. Other than individual clinician or patient choice, it may be that those with more "clear-cut" symptom profiles, such as gastro-oesophageal reflux only or dyspepsia only, were not referred for upper GI endoscopy because the responsible physician did not feel that this would aid their management. This would perhaps explain why those with overlap of both gastro-oesophageal reflux and dyspepsia made up the largest proportion of participants in the study.

Therefore despite the large sample size of over 1100 patients there is the strong possibility of selection bias affecting the results, although when demographic data were compared between those undergoing upper GI endoscopy, and those who did not, there were few differences. There remains the possibility that, if this study were conducted in a population-based sample, there may be greater differences in the spectrum of endoscopic findings between individuals with symptoms of gastro-oesophageal reflux and those with

dyspepsia. However, previous studies conducted in such a setting, [29, 30] as well as a meta-analysis that has examined this issue, [7] have suggested that this is not the case. These findings are echoed by a study conducted in primary care, where patients were referred with upper GI symptoms, as well as a provisional diagnosis from their general practitioner. [31] Here, sensitivities and positive predictive values of symptoms of reflux and dyspepsia for oesophagitis and peptic ulcer, respectively, were less than 60%. A final limitation is that patients presenting with gastro-oesophageal reflux were not required to undergo 24-hour pH studies. It has been estimated that up to 60% of patients with a normal upper GI endoscopy may have pathological acid reflux on pH testing, [32] and consequently there may have been a proportion of patients with non-erosive reflux disease who were labelled incorrectly as having no underlying organic upper GI disease.

Erosive oesophagitis is a recognised complication of gastro-oesophageal reflux, estimated to be present in up to 25% of patients [33], a prevalence similar to that observed among those with reflux symptoms in our study. It is therefore perhaps to be expected that patients with gastro-oesophageal reflux symptoms, or overlap, had a higher prevalence of erosive oesophagitis than those with isolated dyspepsia. As previously discussed, some experts recommend that upper GI endoscopy is performed in patients with gastro-oesophageal reflux symptoms, [19] to rule out Barrett's oesophagus and oesophageal adenocarcinoma. Of more interest, therefore, is the almost identical prevalence of Barrett's oesophagus across the three groups. It has been estimated that the prevalence of histologically-proven Barrett's oesophagus in individuals with reflux is around 6%, [34] similar to the prevalence of 4% we observed. Whether to screen individuals with gastro-oesophageal reflux for Barrett's oesophagus remains debated, as severity of symptoms is not a good predictor for Barrett's oesophagus, [35] although duration of symptoms appears to have a strong positive correlation, [17] and there is also some evidence to suggest that the

prevalence is not significantly different to that in asymptomatic individuals. [36] In addition, although patients with Barrett's oesophagus have an increased risk of developing oesophageal adenocarcinoma, the absolute risk is still low. [37] No cases of oesophageal adenocarcinoma were found in our patient sample, which is perhaps not surprising considering the relatively low, albeit increasing, incidence of the disease. [38, 39] It is, however, interesting to note that the prevalence of peptic ulcer disease and gastric or duodenal erosions were very similar across the three groups, and there were no cases of gastric cancer identified.

These results demonstrate that, with the exception of erosive oesophagitis, there is little difference in the prevalence of underlying organic upper GI disease according to patient-reported symptoms in this selected population of patients. This suggests that the division of upper GI symptoms into the discrete groups of gastro-oesophageal reflux and dyspepsia may be somewhat artificial. This is reflected in the recently published Rome IV criteria, [5] which recognise that, although heartburn is not a dyspeptic symptom per se, it may often co-exist with dyspepsia. Our results also imply that decisions on whether to perform upper GI endoscopy based on presenting symptoms alone are arbitrary. Identification of other factors, including alarm symptoms, as well as the onset or duration of symptoms, may be more useful, although previous studies that have examined the utility of alarm symptoms, and the accuracy of a clinical history in predicting pathology encountered at upper GI endoscopy also suggest that these are of limited utility. [40, 41]

In conclusion, there were few differences in patient characteristics or findings at upper GI endoscopy in over 1000 selected patients with gastro-oesophageal reflux, dyspepsia, or overlap of the two, in secondary care. Although endoscopy is undoubtedly a useful tool in assessing patients presenting with upper GI symptoms, using these to predict underlying organic findings, and therefore identify patient groups who may benefit most from prompt

access to it, is unlikely to be a fruitful approach, particularly for physicians in primary care, where the prevalence of organic disease is low.

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DISCLOSURES

AJI: none to declare. MIP-S: none to declare. PB: none to declare. PM: none to declare. ACF: none to declare.

STATEMENTS OF INTEREST

Guarantor of the article: AC Ford.

Specific author contributions: AJI, MIP-S, PB, PM, and ACF conceived and drafted the study. ACF and MIP-S collected all data. AJI and ACF analysed and interpreted the data. AJI and ACF drafted the manuscript. All authors contributed to and approved the final draft of the manuscript.

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Table 1. Prevalence of Organic Disease at Upper GI Endoscopy in 1167 Included Patients According to Symptom Group.

	Gastro-oesophageal reflux symptoms only (n = 97)	**Dyspepsia Only (n = 571)**	**Overlap of Gastro-oesophageal reflux with dyspepsia (n = 499)**	**P value***
Any organic upper GI disease (%)†	31 (32.0)	124 (21.7)	134 (26.9)	0.035
Erosive oesophagitis (%)	18 (18.6)	41 (7.2)	77 (15.4)	<0.001
LA grade A	11 (61.1)	28 (68.3)	50 (64.9)	
LA grade B	2 (11.1)	5 (12.2)	16 (20.8)	
LA grade C	3 (16.7)	3 (7.3)	6 (7.8)	
LA grade D	2 (11.1)	5 (12.2)	5 (6.5)	0.38
Barrett's oesophagus (%)	4 (4.1)	23 (4.0)	19 (3.8)	0.98
Benign oesophageal stricture (%)	0 (0)	3 (0.5)	3 (0.6)	0.99
Schatzki ring (%)	3 (3.1)	7 (1.2)	4 (0.8)	0.13
Oesophageal candidiasis (%)	0 (0)	5 (0.9)	4 (0.8)	0.99
Eosinophilic oesophagitis (%)	1 (1.0)	2 (0.4)	0 (0)	0.13

Oesophageal squamous cell carcinoma (%)	0 (0)	0 (0)	2 (0.4)	0.34
Oesophageal adenocarcinoma (%)	0 (0)	0 (0)	0 (0)	N/A
Gastric ulcer or erosions (%)	5 (5.2)	33 (5.8)	28 (5.6)	0.97
Gastric carcinoma (%)	0 (0)	0 (0)	0 (0)	N/A
Duodenal ulcer or erosions (%)	2 (2.1)	14 (2.5)	8 (1.6)	0.62
Coeliac disease (%)	0 (0)	19 (3.3)	13 (2.6)	0.15
Upper GI Crohn's disease (%)	0 (0)	1 (0.2)	0 (0)	0.99
H. pylori-positive (%)	7 (7.2)	43 (7.5)	37 (7.4)	0.99

*P value for Pearson χ^2 or Fisher's exact test for comparison of categorical data.

†Some patients had more than one organic finding at upper GI endoscopy.

N/A; not applicable.

Table 2. Prevalence of Organic Disease at Upper GI Endoscopy in 496 Patients with Overlap of Gastro-oesophageal Reflux with Dyspepsia, According to Predominant Symptom.

	Gastro-oesophageal Reflux-predominant (n = 41)	**Dyspepsia-predominant (n = 148)**	**Overlap with no Symptom Predominance (n = 307)**	**P value**
Any organic upper GI disease (%)†	13 (31.7)	34 (23.0)	86 (28.0)	0.40
Erosive oesophagitis (%)	7 (17.0%)	20 (13.5%)	49 (16.0%)	0.75
LA grade A	7 (100.0)	12 (60.0)	32 (65.3)	
LA grade B	0 (0)	5 (25.0)	11 (22.4)	
LA grade C	0 (0)	3(15.0)	3 (6.1)	
LA grade D	0 (0)	0 (0)	5 (10.2)	0.13
Barrett's oesophagus (%)	1 (2.4%)	5 (3.4%)	12 (3.9%)	0.99
Benign oesophageal stricture (%)	0 (0%)	1 (0.7%)	2 (0.7%)	0.99
Schatzki ring (%)	0 (0%)	3 (2.0%)	1 (0.3%)	0.17
Oesophageal candidiasis (%)	0 (0%)	2 (1.4%)	2 (0.7%)	0.72

Eosinophilic oesophagitis (%)	0 (0%)	0 (0%)	0 (0%)	N/A
Oesophageal squamous cell carcinoma (%)	0 (0%)	1 (0.7%)	1 (0.3%)	0.62
Oesophageal adenocarcinoma (%)	0 (0%)	0 (0%)	0 (0%)	N/A
Gastric ulcer or erosions (%)	3 (7.3%)	5 (3.4%)	20 (6.5%)	0.33
Gastric carcinoma (%)	0 (0%)	0 (0%)	0 (0%)	N/A
Duodenal ulcer or erosions (%)	2 (4.9%)	2 (1.4%)	4 (1.3%)	0.23
Coeliac disease (%)	4 (9.8%)	2 (1.4%)	7 (2.3%)	0.03
Upper GI Crohn's disease (%)	0 (0%)	0 (0%)	0 (0%)	N/A
H. pylori-positive (%)	4 (9.8)	9 (6.1)	24 (7.8)	0.68

*P value for Pearson χ^2 or Fisher's exact test for comparison of categorical data.

†Some patients had more than one organic finding at upper GI endoscopy.

N/A; not applicable.

FIGURE LEGENDS.

Figure 1. Flow of Study Participants.

Figure 2. Degree of Overlap Between Gastro-oesophageal Reflux and Dyspepsia Symptoms in 1167 Patients.