

Diagnostic yield from symptomatic gastroscopy in the UK: British Society of Gastroenterology analysis using data from the National Endoscopy Database

Abstract

Objective

This national analysis aimed to calculate the diagnostic yield from gastroscopy for common symptoms, guiding improved resource utilisation.

Design

A cross-sectional study was conducted of diagnostic gastroscopies between 01/03/2019-29/02/2020 using the UK National Endoscopy Database (NED). Mixed-effects logistic regression models were used, incorporating random (endoscopist) and fixed (symptoms, age, and sex) effects upon two dependent variables (endoscopic cancer; Barrett's oesophagus (BO) diagnosis). Adjusted positive predictive values (aPPVs) were calculated.

Results

382,370 diagnostic gastroscopies were analysed; 30.4% were performed in patients aged <50 and 57.7% on female patients. The overall unadjusted PPV for cancer was 1.0% (males 1.7%; females 0.6%, $p < 0.01$). Other major pathology was found in 9.1% of procedures, whereas 89.9% reported only normal findings or minor pathology (92.5% in females; 94.6% in patients <50).

Highest cancer aPPVs were reached in the over 50s (1.3%), in those with dysphagia (3.0%), or weight loss plus another symptom (1.4%). Cancer aPPVs for all other symptoms were below 1%, and for those under 50, remained below 1% regardless of symptom. Overall, 73.7% of gastroscopies were carried out in patient groups where aPPV cancer was <1%.

The overall unadjusted PPV for BO was 4.1% (males 6.1%; females 2.7%, $p < 0.01$). The aPPV for BO for reflux was 5.8% and ranged from 3.2%-4.0% for other symptoms.

Conclusions

Cancer yield was highest in elderly male patients, and those over 50 with dysphagia. Three quarters of all gastroscopies were performed on patients whose cancer risk was <1%, suggesting inefficient resource utilisation.

What is already known on this topic

- Gastroscopies contribute significantly to the UK endoscopy workload. Endoscopy services are increasingly struggling to meet this demand in the UK, risking delay to time-critical diagnoses such as cancer. Utilising resource more efficiently, by prioritising high risk patients whilst reducing low yield endoscopy, would help resolve this. To inform decision-making around service re-configuration, large-scale high-quality data is needed to establish the relationship between symptoms and the yield of significant pathology.

What this study adds

- In the UK, 66% of symptomatic gastroscopies were performed to investigate the symptoms with the lowest risk of cancer: dyspepsia, reflux, and anaemia. Additionally, a third were performed on patients under 50, despite very low risk of significant pathology (cancer 0.1%, Barrett's oesophagus 1.9%), and more were performed on female patients (58%), despite higher pathology risk in male patients: broadly speaking, a male's risk of cancer (or Barrett's) is equivalent to a female 20 years older.

How this study might affect research, practice or policy

- Data from this novel national database enables the risk prediction of cancer and Barrett's oesophagus based on patient symptoms, age, and sex. The findings identify patient groups that would benefit from gastroscopy assessment, as well as those who could be appropriately triaged towards less urgent, alternative, or even no investigation. By leveraging this data, endoscopy services can enhance referral pathways and optimise the utilisation of available resources, helping alleviate current service pressures and improving patient management.

Introduction

UK endoscopy services are struggling to cope with demand, with many patients waiting over 6 weeks for urgent endoscopy appointments which should be scheduled within two weeks. [1] This constitutes a major problem, as delays in endoscopy appointments can result in later-stage diagnoses of upper gastrointestinal cancers, contributing to lower survival rates in the UK compared to (some) other developed countries. [2-4] The prolonged waiting period also has a significant psychological impact on patients, causing increased distress and decreased quality of life, particularly for those who fear a cancer diagnosis. [5] The COVID pandemic has compounded these problems, [6] which have roots in ineffective workforce planning [7] and limited endoscopy facilities within the resource-constrained NHS system, combined with increasing demand driven by an ageing population. [8]

To enhance patient outcomes, UK endoscopy services must adopt a more efficient approach, shifting away from low-yield endoscopy and optimising resource utilisation through the identification and prioritisation of higher-risk patients. Understanding current practices, including volume, indications, and diagnostic yields, is crucial to this effort. The UK National Endoscopy Database (NED) - which 95% of UK endoscopy services engage with [9]) - can play a key role, offering large-scale data in near real-time, obtained automatically from electronic endoscopy reports. [10]

The primary aim of this study was to use data from the NED to evaluate diagnostic yield for gastroscopies performed to investigate patient symptoms, overall and for different patient age-groups and sex. This included calculation of positive predictive value (PPV) of common upper GI symptoms (at different patient ages and sex) for identifying cancer and Barrett's oesophagus (BO) at gastroscopies. The goals were to identify opportunities for future capacity optimisation, including helping guide future referral pathways, and to provide information to support decision-making among patients and healthcare professionals regarding the necessity of undergoing gastroscopy.

Methods

Data source

Prospectively gathered data uploaded to NED relating to endoscopies conducted from 1st Mar 2019 – 29th Feb 2020 was analysed; this time period was selected to avoid the analysis being impacted by the effects of the COVID-19 pandemic. [6] During or after each endoscopic procedure, clinical teams enter information onto their local endoscopy reporting system; this data is automatically uploaded to the National Endoscopy Database (NED) using a standardised data schema developed following data mapping and validation exercises. [10] Monitoring of each reporting system revealed that over 98% of

reports were successfully uploaded to NED. [9] As the NED data is anonymised and not linked to histology, the diagnosis recorded is based solely on the endoscopic findings.

The analysis dataset included gastroscopy procedures in patients aged 18 and older. Duplicate procedure uploads were identified and excluded (with the index procedure retained) as were procedures conducted on patients over 99 years old (as such cases were likely to be data entry errors), and the small number of procedures where patient sex was unclassified (Figure 1). Abandoned procedures, including gastroscopies that where failed intubation was recorded, were also excluded.

NED offers the flexibility of free-text entry in both the indication for referral and diagnosis fields, in addition to pre-set input options from the standardised data schema. To prevent omission of relevant data free-text entries were carefully scrutinised using the txttool utility in Stata [7] and, where appropriate, re-coded to corresponding NED terms for indication and diagnosis. Following this, if endoscopies did not include a recorded indication or diagnosis, they were excluded.

Figure 1. Flowchart illustrating creation of analysis dataset.

Figure 2. Positive predictive value of Barrett's oesophagus (BO) and cancer by patient age group for female and patient patients (with 95% CIs).

Data coding: indications, symptoms, and diagnoses

Each gastroscopy was classified according to the recorded indication for the procedure. If multiple indications were present classification was determined by severity, with the hierarchy as follows: Upper GI bleed > Therapeutic/Emergency > Screening and Surveillance > Abnormal prior investigation > Symptomatic. For example, if a procedure included BO surveillance and dyspepsia as indications it was categorised as “Screening and Surveillance.” As the analysis focused on gastroscopies performed to investigate patient symptoms in an out-patient setting, those conducted for other indications were excluded. Additional information on the exclusions can be found in Figure 1.

In NED, the indications fields may include multiple symptoms. For analysis, less frequently recorded symptoms were combined with more common ones when appropriate (e.g., odynophagia & dysphagia, abdominal pain & dyspepsia). For the primary analysis, gastroscopies were classified by symptom - as described in Table 1 – using a hierarchy of “severity”, namely: Dysphagia, weight loss, anaemia, nausea / vomiting, reflux, dyspepsia; for example, if dysphagia and dyspepsia were both recorded as indications the symptom was grouped as dysphagia. As current referral guidelines for urgent gastroscopy include the combination of weight loss and other GI symptoms [11] as opposed to weight loss alone - this symptom was split as per Table 1. In secondary analyses, each symptom was analysed individually and in conjunction with another symptom (Supplemental Table 1).

The outcome variables for the analyses related to endoscopic diagnoses. Since NED offers options to record multiple diagnoses for a procedure to reflect the diverse pathology encountered, similar terms were combined (i.e., non-erosive gastritis and erosive gastritis combined to gastritis), and resultant terms were then grouped based upon severity (Table 1). Multiple diagnosis groups could be assigned to a procedure: for example, if a gastroscopy reported both ‘duodenitis’ and ‘gastric ulcer’ as diagnoses it would be included in both the ‘minor pathology’ and ‘ulcer’ outcome groups.

Table 1. Explanatory and outcome variables.

(a)

(A) Hierarchical categorisation of gastroscopies by symptoms, with descriptions			
Symptom groups	Hierarchy	Description / NED indication term in each group	
Dysphagia	1	Indications include dysphagia, either alone or in combination with other symptoms	
Weight loss & other symptom(s)	2	Indications include weight loss and other symptoms (excluding dysphagia)	
Weight loss	3	Weight loss as sole indication	
Anaemia	4	Indications include anaemia, either alone or in combination with other symptoms (excluding dysphagia & weight loss)	
Nausea & Vomiting	5	Indications include nausea/vomiting, either alone or in combination with reflux/dyspepsia	
Reflux	6	Reflux, either alone or in combination with dyspepsia	
Dyspepsia	7	Dyspepsia as sole indication	
(B) Grouping of diagnoses based on severity.			
Diagnosis	Description / NED diagnosis terms in each group		
Normal	Normal		
Minor pathology	Angiodysplasia	Gastric polyp(s)	Oesophageal Candidiasis
	Duodenal diverticulum	Gastritis	Oesophageal diverticulum
	Duodenal Polyp	Gastropathy-Portal Hypertensive	Oesophageal Polyp
	Duodenitis	Hiatus Hernia	Oesophagitis-Reflux
	Extrinsic Compression	Mallory-Weiss tear	Schatzki ring
Major pathology	Achalasia	Gastric Varices	Pyloric Stenosis
	Fistula (gastric/oesophageal)	Oesophageal Stricture – Benign	Pharyngeal Pouch
	Foreign Body	Oesophageal Varices	
	GAVE	Oesophagitis – Eosinophilic	
Ulcer	Duodenal Ulcer	Gastric Ulcer	Oesophageal Ulcer
Barrett's oesophagus	Barrett's Oesophagus		
Cancer	Duodenal Tumour – malignant	Gastric Tumour - malignant	
	Oesophageal Tumour – malignant	Unspecified Tumour (free text)	

*The symptom groups were mutually exclusive and each procedure could only be recorded in one category. The diagnosis groups were not mutually exclusive, meaning that each procedure could be classified under multiple diagnosis groups, except for the "normal" category

Statistical Analysis

Descriptive statistics (expressed as percentages unless otherwise noted) were applied to summarise the patient demographics (age, sex) and symptom groups. Pearson's chi-square test was used to identify associations between categorical variables. Patient demographics and symptom data groups were compared by health sector (NHS or Independent sector). As many endoscopies conducted within independent sector sites are on behalf of the NHS, [2] with providers being reimbursed by NHS services to enhance capacity and alleviate waiting times (i.e. outsourcing), the primary analysis encompassed data from all participating sites. Secondary analysis was conducted focusing specifically on data uploaded from NHS sites.

PPVs were presented alongside 95% confidence intervals, calculated using the Wilson method. [12] The unadjusted PPV of each diagnosis group and the proportion of gastroscopies performed within each age group (categorised as 18-39, 40-49, 50-59, 60-69, 70-79, and 80-99 years old) was calculated, and subsequently analysed by patient sex.

The impact of symptoms, patient sex, and patient age upon the PPV of cancer - and separately BO - was examined using two-level mixed effects logistic regression models. [13] These accounted for the non-independence of procedures (which are clustered within endoscopists) by fitting endoscopist as a random effect, with symptoms, patient sex, and patient age-group as fixed effects upon the binomial dependent variable (cancer, BO). The primary models included patient age by group (18-39, 40-49, etc); a subsequent analysis explored the impact of an age cut-off of 50, and for that analysis, regression was performed with age a dichotomous variable (aged less than 50, aged 50 or more). Postestimation commands were used to calculate the marginal means of the dependent variable based on co-variables, with results displayed as adjusted PPV (aPPV) with 95% confidence intervals. Analysis was then rerun using the additional symptom combinations (secondary analyses; Supplemental Table 1) within the random effects upon the dependent variable of cancer. Finally, regression was repeated restricting consideration to gastroscopies uploaded from NHS sites (sensitivity analyses; Supplemental Table 2).

Analyses was performed using Microsoft Excel (Microsoft Corp, Redmond, WA, USA) and STATA v17 (StataCorp LP, College Station, Texas, USA).

Approvals

As no patient identifiable information was used this project was assessed as not requiring ethical approval by the North Tees and Hartlepool NHS Foundation Trust Caldicott guardian. The Research and Development Department at North Tees and Hartlepool NHS Foundation Trust approved the

project. The analysis was supported by the Joint Advisory Group for gastrointestinal endoscopy and the British Society of Gastroenterology (BSG).

Results

Following exclusions (Figure 1), data from 382,370 gastroscopies performed to investigate patient symptoms were analysed. These were performed by 4,320 endoscopists, with most (80.0%) performed within NHS sites. Slightly more than half of patients were female (57.7%); 30.4% were performed on patients aged under 50.

Nearly half of symptomatic gastroscopies were performed to investigate symptoms of dyspepsia or reflux (47.9%), with the next most frequent indications being dysphagia (19.7%) and anaemia (18.6%). Most gastroscopies (77.3%) recorded a single symptom indication, 19.9% recorded two, and 2.8% recorded three or more symptoms. Further details on symptom combinations are detailed in Supplemental Table 1.

Symptomatic gastroscopies conducted at NHS sites were performed on older patients compared to those conducted at the independent sector (median age 62 vs. 52, $p < 0.01$). A higher proportion of gastroscopies performed at NHS sites were to investigate dysphagia or weight loss (31.1% vs. 12.3%, $p < 0.01$). Almost three-quarters of gastroscopies performed at the independent sector were undertaken to investigate reflux or dyspepsia (73.9%), compared to 41.4% for those performed at NHS sites ($p < 0.01$).

Table 2. Characteristics of patients and symptoms present during gastroscopies performed to investigate symptoms in both NHS and independent sector sites

	Overall		National health service sites		Independent sector sites	
	n		n		n	
Gastroscopies	382,370		305,722	80.0%	76,648	20.0%
Endoscopy Sites	398		231		166	
Endoscopists	4,320		3,719		1,214	
Female sex (%)	220,667	57.7%	176,928	57.9%	43,739	57.1%
Median age (Interquartile range)	59	(46-72)	62	(49-73)	52	(39-63)
Patient age-groups (% within each group)	n	%	n	%	n	%
18-39	61,818	16.2%	42,413	13.9%	19,405	25.3%
40-49	54,189	14.2%	38,833	12.7%	15,356	20.0%
50-59	75,902	19.9%	58,662	19.2%	17,240	22.5%
60-69	77,468	20.3%	64,647	21.2%	12,821	16.7%
70-79	74,863	19.6%	65,805	21.5%	9,058	11.8%
80-99	38,130	10.0%	35,362	11.6%	2,768	3.6%
Symptom groups (n, % within each group)*	n	%	n	%	n	%
1 – Dysphagia	75,152	19.7%	68,316	22.4%	6,836	8.9%
2 - Weight loss & other symptom(s)	19,437	5.1%	17,833	5.8%	1,604	2.1%
3 - Weight loss	10,031	2.6%	9,020	3.0%	1,011	1.3%
4 – Anaemia	70,962	18.6%	65,094	21.3%	5,868	7.7%
5 - Nausea & Vomiting	23,736	6.2%	19,037	6.2%	4,699	6.1%
6 – Reflux	77,250	20.2%	51,926	17.0%	25,324	33.0%
7 – Dyspepsia	105,802	27.7%	74,496	24.4%	31,306	40.8%

*Symptom groups are hierarchical, as per table 1, and each gastroscopy can only be included in a single group.

Cancer was reported in 3,968 gastroscopies, with an overall unadjusted PPV of 1.0% (95% CI 1.0-1.1). Cancer PPV was higher in NHS sites compared to independent sector sites (1.2% (95% CI 1.2-1.3) vs 0.3% (95% CI 0.2-0.3), $p<0.01$) 89.9% (95% CI 89.8-90.0) of symptomatic gastroscopies were reported as normal or identifying only minor pathology; this figure was higher in female than male patients (female: 92.5% (95% CI 92.4-92.6); male 86.3% (95% CI 86.1-86.4)). For patients under 50 years of age, only 5.4% of gastroscopies reported anything other than normal findings or minor pathology, and cancer was particularly uncommon (0.1%, 95% CI 0.1-0.1). The unadjusted PPV of major pathologies increased with age and was higher in male patients, as shown in Table 3 and Figure 2.

Table 3. Proportion of symptomatic gastroscopies recording each diagnosis group, by patient age-group and sex (presented as unadjusted positive predictive value with 95% CIs)

Overall									
Patient age-group	Procedures	% within age-group	Normal	Minor pathology	Major pathology	Ulcer	Barrett's Oesophagus	Cancer	Normal/ Minor pathology ONLY
18–39	61,818	16.2%	49.8% (49.4-50.2)	48.5% (48.1-48.9)	1.2% (1.1-1.3)	2.0% (1.9-2.1)	1.4% (1.4-1.5)	<0.1% (0.0-0.1)	95.4% (95.3-95.6)
40–49	54,189	14.2%	42.9% (42.5-43.3)	55.0% (54.6-55.4)	1.3% (1.2-1.4)	2.7% (2.5-2.8)	2.4% (2.3-2.6)	0.2% (0.2-0.3)	93.5% (93.3-93.7)
50–59	75,902	19.9%	36.2% (35.8-36.5)	61.0% (60.7-61.3)	1.6% (1.5-1.7)	3.2% (3.1-3.3)	4.0% (3.9-4.2)	0.6% (0.6-0.7)	90.9% (90.7-91.1)
60–69	77,468	20.3%	31.7% (31.4-32.0)	64.6% (64.3-64.9)	2.2% (2.1-2.3)	3.6% (3.4-3.7)	5.0% (4.9-5.2)	1.2% (1.2-1.3)	88.5% (88.2-88.7)
70–79	74,863	19.6%	29.1% (28.8-29.4)	66.5% (66.1-66.8)	2.9% (2.8-3.0)	3.9% (3.8-4.0)	5.7% (5.6-5.9)	1.9% (1.8-2.0)	86.2% (85.9-86.5)
80–99	38,130	10.0%	28.2% (27.7-28.6)	65.9% (65.4-66.4)	4.3% (4.1-4.5)	4.3% (4.1-4.5)	5.9% (5.7-6.2)	2.6% (2.4-2.8)	83.6% (83.2-83.9)
Overall	382,370	100.0%	36.3% (36.1-36.4)	60.4% (60.3-60.6)	2.1% (2.1-2.2)	3.3% (3.2-3.3)	4.1% (4.0-4.2)	1.0% (1.0-1.1)	89.9% (89.8-90.0)
Female Patients									
Patient age-group	Procedures	% within age-group	Normal	Minor pathology	Major pathology	Ulcer	Barrett's Oesophagus	Cancer	Normal/ Minor pathology ONLY
18–39	35,511	16.1%	55.5% (55.0-56.1)	43.2% (42.6-43.7)	0.8% (0.8-0.9)	1.6% (1.4-1.7)	0.8% (0.7-0.9)	<0.1% (0.0-0.1)	96.8% (96.7-97.0)
40–49	32,396	14.7%	47.1% (46.5-47.6)	51.3% (50.7-51.8)	1.0% (0.9-1.1)	2.1% (2.0-2.3)	1.4% (1.3-1.5)	0.1% (0.0-0.1)	95.5% (95.2-95.7)
50–59	45,203	20.5%	38.7% (38.2-39.1)	59.3% (58.8-59.7)	1.2% (1.1-1.3)	2.8% (2.6-2.9)	2.5% (2.4-2.7)	0.3% (0.2-0.3)	93.5% (93.3-93.7)
60–69	44,635	20.2%	33.2% (32.8-33.6)	64.2% (63.7-64.6)	1.8% (1.7-1.9)	3.0% (2.8-3.1)	3.3% (3.2-3.5)	0.6% (0.5-0.6)	91.6% (91.3-91.8)
70–79	42,086	19.1%	29.3% (28.9-29.7)	67.5% (67.1-68.0)	2.6% (2.4-2.8)	3.4% (3.3-3.6)	3.9% (3.7-4.0)	1.0% (0.9-1.1)	89.5% (89.2-89.8)
80–99	20,836	9.4%	28.2% (27.6-28.8)	67.0% (66.3-67.6)	4.4% (4.1-4.7)	3.8% (3.5-4.0)	4.2% (4.0-4.5)	1.9% (1.7-2.1)	86.3% (85.8-86.7)
Overall	220,667	100.0%	38.7% (38.5-38.9)	58.8% (58.6-59.0)	1.8% (1.7-1.8)	2.7% (2.7-2.8)	2.7% (2.6-2.7)	0.6% (0.5-0.6)	92.5% (92.4-92.6)
Male Patients									
Patient age-group	Procedures	% within age-group	Normal	Minor pathology	Major pathology	Ulcer	Barrett's Oesophagus	Cancer	Normal/ Minor pathology ONLY
18–39	26,307	16.3%	42.2% (41.6-42.8)	55.7% (55.1-56.3)	1.6% (1.5-1.8)	2.6% (2.4-2.8)	2.4% (2.2-2.6)	0.1% (0.0-0.1)	93.5% (93.2-93.8)
40–49	21,793	13.5%	36.6% (36.0-37.3)	60.6% (60.0-61.3)	1.7% (1.6-1.9)	3.5% (3.2-3.7)	4.0% (3.7-4.3)	0.4% (0.4-0.5)	90.7% (90.3-91.1)
50–59	30,699	19.0%	32.6% (32.1-33.1)	63.5% (63.0-64.0)	2.3% (2.1-2.4)	3.8% (3.6-4.0)	6.2% (6.0-6.5)	1.2% (1.1-1.3)	87.0% (86.6-87.4)
60–69	32,833	20.3%	29.7% (29.2-30.2)	65.2% (64.7-65.7)	2.8% (2.6-3.0)	4.4% (4.2-4.6)	7.4% (7.1-7.6)	2.1% (2.0-2.3)	84.2% (83.8-84.6)
70–79	32,777	20.3%	28.8% (28.4-29.3)	65.1% (64.6-65.6)	3.3% (3.1-3.5)	4.5% (4.3-4.8)	8.2% (7.9-8.5)	2.9% (2.8-3.1)	82.0% (81.6-82.4)
80–99	17,294	10.7%	28.2% (27.6-28.9)	64.7% (64.0-65.4)	4.2% (3.9-4.5)	5.0% (4.7-5.3)	8.0% (7.6-8.4)	3.4% (3.2-3.7)	80.3% (79.7-80.9)
Overall	161,703	100.0%	32.9% (32.7-33.1)	62.7% (62.4-62.9)	2.6% (2.5-2.7)	4.0% (3.9-4.1)	6.1% (6.0-6.2)	1.7% (1.6-1.8)	86.3% (86.1-86.4)

*Note: Results are not hierarchical; each procedure may have multiple diagnoses recorded and these procedures have been included in each diagnostic group.

The adjusted odd ratio (aOR) of cancer being reported increased with patient age (Table 4) and was 3-fold higher in males than females (aOR 3.0, 95% CI 2.8-3.2). A gastroscopy carried out to investigate dysphagia was over ten times as likely to record a cancer as one investigating dyspepsia (aOR 10.1, 95%CI 8.8-11.5). Odds of cancer were also significantly raised in procedures conducted to investigate weight loss plus other symptoms, weight loss alone, nausea/vomiting and anaemia.

Table 4. Mixed-effects logistic regression of the association of reporting cancer from gastroscopies by patient age group, patient sex, and symptoms (with endoscopist variation as random effect): numbers of procedures and cancers, adjusted odds ratios (aOR), with 95% CIs and p values

Patient age group	Procs	Cancers	aOR*	(95% CI)	p
18-39	61,818	29	0.05	(0.04-0.07)	<0.01
40-49	54,189	115	0.20	(0.16-0.24)	<0.01
50-59	75,902	488	0.55	(0.49-0.61)	<0.01
60-69	77,468	952	1.00	-	
70-79	74,863	1,392	1.42	(1.30-1.54)	<0.01
80-99	38,130	992	1.70	(1.55-1.87)	<0.01
Patient Sex					
Female	220,667	1,239	1.00	-	
Male	161,703	2,729	2.95	(2.75-3.16)	<0.01
Hierarchical symptom groups					
1 – Dysphagia	75,152	2,623	10.08	(8.83-11.50)	<0.01
2 - Weight loss & other symptom(s)	19,437	305	4.35	(3.67-5.16)	<0.01
3 - Weight loss	10,031	89	2.21	(1.73-2.82)	<0.01
4 – Anaemia	70,962	451	1.39	(1.19-1.63)	<0.01
5 - Nausea/Vomiting	23,736	116	2.21	(1.77-2.76)	<0.01
6 – Reflux	77,250	130	0.68	(0.55-0.84)	<0.01
7 – Dyspepsia	105,802	254	1.00	-	
Endoscopist variation			0.27	(0.22-0.34)	

*ORs mutually adjusted for variables in the table. Symptoms defined as per table 1.

The 75,152 (19.7% overall) gastroscopies performed to investigate dysphagia identified 2,623 cancers (66.1% of all cancers). The adjusted PPV (aPPV) for cancer in gastroscopies performed to investigate dysphagia was 6.8% in males aged 50 and above; it only exceeded 3% in females aged 70 and above.

The 254,014 gastroscopies performed to investigate anaemia, reflux, or dyspepsia represented two-thirds of all symptomatic gastroscopies (66.4%) and identified 835 cancers (21.0% of all cancers). For patients referred with these symptoms, aPPVs for cancer were low overall (anaemia: 0.4%, dyspepsia 0.3%, and reflux 0.2%) and cancer aPPV only exceeded 1% among males aged over 70 with anaemia (Table 5).

The aPPV for cancer when weight loss was combined with another symptom was double that from weight loss alone (aPPV 1.4% vs 0.7%). The aPPV cancer for weight loss as a lone symptom did not reach 3% in any patient group and was below 1% within all female age-groups and males aged <60. Most symptomatic gastroscopies (73.7%) were carried out in patient groups where aPPV cancer was under 1%, including 82.0% performed upon female patients and 62.2% performed upon male patients.

Further information is found on Table 5 (Supplemental Table 3 shows the 95% confidence intervals for the aPPVs in Table 5). The results of the secondary analysis considering other symptom combinations can be found in Supplemental Table 1. In the sensitivity analyses, the adjusted aPPVs from NHS sites only differed little from the overall PPVs (Supplemental table 2).

Table 5. Adjusted positive predictive values (aPPVs) for identifying cancer from symptomatic gastroscopies, by symptom, age group and patient sex, based on modelled output from regression analysis: overall and by sex

Symptoms	Procs	Cancers	aPPV Cancer by symptom			Female aPPV Cancer		Male aPPV Cancer		Female aPPV Cancer by age-group						Male aPPV Cancer by age-group					
			Female	Male	Overall	Age <50	Age 50+	Age <50	Age 50+	18-39	40-49	50-59	60-69	70-79	80-99	18-39	40-49	50-59	60-69	70-79	80-99
Dysphagia	75,152	2,623	1.72%	4.78%	3.04%	0.29%	2.42%	0.85%	6.78%	0.12%	0.44%	1.21%	2.18%	3.05%	3.63%	0.34%	1.29%	3.46%	6.10%	8.37%	9.84%
Weight loss and other	19,437	305	0.76%	2.17%	1.37%	0.13%	1.10%	0.38%	3.18%	0.05%	0.19%	0.53%	0.95%	1.35%	1.61%	0.15%	0.56%	1.53%	2.75%	3.84%	4.56%
Weight loss	10,031	89	0.39%	1.13%	0.71%	0.07%	0.57%	0.20%	1.68%	0.03%	0.10%	0.27%	0.49%	0.69%	0.83%	0.07%	0.29%	0.79%	1.42%	2.00%	2.39%
Nausea / vomiting	23,736	116	0.39%	1.13%	0.71%	0.06%	0.50%	0.17%	1.47%	0.03%	0.10%	0.27%	0.49%	0.69%	0.83%	0.07%	0.29%	0.79%	1.42%	2.00%	2.39%
Anaemia	70,962	451	0.25%	0.72%	0.45%	0.04%	0.38%	0.13%	1.11%	0.02%	0.06%	0.17%	0.31%	0.44%	0.52%	0.05%	0.18%	0.50%	0.90%	1.27%	1.52%
Dyspepsia	105,802	254	0.18%	0.52%	0.32%	0.03%	0.22%	0.08%	0.65%	0.01%	0.04%	0.12%	0.22%	0.31%	0.38%	0.03%	0.13%	0.36%	0.65%	0.92%	1.10%
Reflux	77,250	130	0.12%	0.35%	0.22%	0.02%	0.15%	0.05%	0.44%	0.01%	0.03%	0.08%	0.15%	0.21%	0.26%	0.02%	0.09%	0.24%	0.44%	0.63%	0.75%

Table 6 shows that the aOR of diagnosing BO increased with patient age. Moreover, male patients were over twice as likely as females to be diagnosed with BO (aOR 2.4, 95% CI 2.3-2.5). Patients with reflux symptoms had the highest risk of being diagnosed with BO, with an aOR of 1.9 (95% CI 1.8-2.0) when compared to those with dyspepsia. The adjusted odds of diagnosing BO were similar for all other symptoms (Table 6).

Table 6. Mixed-effects logistic regression of the association of reporting Barrett's oesophagus from gastroscopies by patient age group, patient sex, and symptoms (with endoscopist variation as random effect): numbers of procedures and cancers, adjusted odds ratios (OR), with 95% CIs and p values

Patient age group	Procs	Barrett's oesophagus	OR	(95% CI)	p
18-39	61,818	893	0.27	(0.25-0.29)	<0.01
40-49	54,189	1,324	0.47	(0.44-0.50)	<0.01
50-59	75,902	3,045	0.80	(0.76-0.84)	<0.01
60-69	77,468	3,906	1.00		
70-79	74,863	4,302	1.15	(1.10-1.21)	<0.01
80-99	38,130	2,266	1.21	(1.14-1.28)	<0.01
Patient Sex					
Female	220,667	5,854	1.00		
Male	161,703	9,882	2.41	(2.33-2.49)	<0.01
Hierarchical symptom groups					
1 – Dysphagia	75,152	3,222	1.18	(1.12-1.25)	<0.01
2 - Weight loss & other symptom(s)	19,437	771	1.08	(1.00-1.18)	0.06
3 - Weight loss	10,031	417	1.10	(0.98-1.22)	0.10
4 – Anaemia	70,962	3,522	1.26	(1.19-1.33)	<0.01
5 - Nausea/Vomiting	23,736	704	1.14	(1.05-1.24)	<0.01
6 – Reflux	77,250	4,081	1.89	(1.80-1.99)	<0.01
7 – Dyspepsia	105,802	3,019	1.00		
<i>Endoscopist variation</i>			0.44	(0.40-0.49)	

*ORs mutually adjusted for variables in the table. Symptoms defined as per table 1.

The aPPV of BO was highest in gastroscopies performed to investigate reflux and increased with patient age (Supplemental Table 7). The overall aPPV from reflux was 5.8% and reached 10.0% in males aged 50+. The aPPVs of BO were similar for other symptoms, ranging from 3.2% for dyspepsia to 4.0% for anaemia.

The aPPV of BO was above 5% for all symptoms in males aged 50 and above. However, for female patients, the aPPV of BO remained under 5% for all age-groups and symptoms, except for reflux in those aged over 70.

Discussion

In the UK, endoscopy activity and diagnostic yields (in both the NHS and Independent Sectors) can now be monitored in a timely manner through the NED, enabling the analysis of endoscopic indications. This analysis indicates that in the year before the COVID-19 pandemic, two-thirds of UK gastroscopies were performed to examine patient symptoms, with a third of these being conducted on patients under 50, even though only 5% of this age group overall (and 4% of females) had significant pathology. Moreover, almost two-thirds of symptomatic gastroscopies were performed to investigate symptoms with the lowest PPVs for cancer – anaemia, reflux, and dyspepsia. This included 82% of those undertaken in the independent sector.

This study reaffirms that while upper GI symptoms are common, they often don't indicate significant medical conditions, especially in younger patients. Our findings expand on previous studies with smaller cohorts, [14] showing that gastroscopies in those under 50 recorded a low yield of significant pathology and almost no cancer. For the first time using a nationwide dataset, our results corroborate the weak association between upper GI symptoms (excluding dysphagia) and cancer risk. [14, 15] Strikingly, two-thirds of symptomatic gastroscopies were conducted on patients exhibiting symptoms with the lowest cancer PPV: reflux (0.2%), dyspepsia (0.3%), and anaemia (0.5%). Additionally, most were performed on female patients, despite those performed on male patients having higher PPV of all significant pathology; notably, the PPV for cancer was three-times higher in males than females: the cancer risk for a male was roughly equivalent to that of a female 20 years older. This prompts reconsideration of whether procedures, especially in young female patients with low-risk symptoms, are always justified.

The challenge is identifying with a high degree of confidence those patients who do not need to be investigated. Even negative gastroscopies can have value, providing relief of patient anxiety, reductions in future primary care consultations, and rationalisation of medications post-endoscopy. [16, 17] Moreover, missing cancer in younger patients has the potential to alter subsequent healthcare professional behaviour. [18] Consequently, as this analysis indicates, opting for a gastroscopy even in patients with low-risk GI symptoms is frequently the favoured choice among healthcare professionals and patients.

But this approach poses challenges, especially in resource-limited settings like the NHS where gastroscopy availability is constrained. Our analysis reveals that gastroscopies on patients over 60 are three times more likely to detect significant pathology and 15 times more likely to identify cancer than those under 50. Yet, a large number of gastroscopies are performed on younger patients, even as many endoscopy services struggle to meet urgent cancer wait-time targets. [19] Delays in cancer diagnoses also have consequences for patients and the health system (e.g. extended period of anxiety,

later stage diagnosis and – potentially - more aggressive and more costly, treatment); these consequences need to be weighed against the perceived advantages of referring all with symptoms, irrespective of likely risk of significant pathology.

The solution begins with improving patient triage. UK guidelines state that young patients with ulcer-like symptoms should undergo a ‘test and treat’ approach for H.Pylori before referral for gastroscopy – an approach found to be cost-effective, [20] reduce future incidence of gastric cancer, [21] and effectively treat ulcer and non-ulcer dyspepsia. [22] Despite initial hesitancy from healthcare professionals, local audit feedback improved referral quality and decreased volume by guiding those making referrals. [23] Triage could be further optimised by incorporating validated risk scores to referrals – better grading procedure urgency and whether an gastroscopy is required at all. [24] These relatively simple measures, if routinely implemented, would reduce endoscopy workload and reduce the burden of unwarranted referrals, [25, 26] while triaging patients more likely to benefit from urgent assessment.

Revising guidelines is a further avenue for reducing the number of low-yield endoscopies. Current UK guidance does not advise endoscopic assessment in young people with non-alarm symptoms, [27] but this is at odds with Rome IV criteria, which recommends ruling out organic pathology as part of its diagnostic criteria for functional dyspepsia. [28] The limited diagnostic yield in young patients with dyspepsia suggests Rome IV should be revised and a more pragmatic approach applied.

The risk in decreasing the volume of gastroscopies performed in that survival from upper GI cancers in the UK already lags behind several neighbouring countries, [4] combined with high rates of post-gastroscopy upper GI cancer (POUGIC). [29] We would hope that the removal of low-yield OGDs will both change the endoscopist mindset from “most tests are normal, I won’t find anything” to “these are high-risk patients so I need to be vigilant”, and free up endoscopic capacity to permit sufficient time for a more thorough examination, which could improve the quality of OGDs and result in improvements in POUGIC rates and cancer survival.

Results also support previous smaller analyses showing that those with upper GI symptoms are at higher risk of BO than those without symptoms – with 4% of symptomatic gastroscopies reporting BO on the background of population prevalence estimated at 0.5-2%. They also replicate the male:female ratio of 2–3:1 and roughly 20-year lag between male and equivalent female prevalence. [30, 31] However, even in the highest risk patient group, males over 50 with reflux, the PPV only reached 10%, and most of the BO reported – 74% - was from the 80% of gastroscopies referred for symptoms other than reflux. This illustrates the primary limitation of current BO surveillance strategies: the inability to accurately identify a target population, meaning most BO cases go undiagnosed, and over 90% of oesophageal cancers are detected without prior BO diagnosis. [32] The development of minimally invasive alternatives to gastroscopy, such as cytosponge, holds potential for overcoming

this limitation in the future by providing widespread screening that is acceptable to both patients and health system payers. [33-35] There is also increasing evidence of its role in investigating all oesophageal symptoms, [36] potentially directing many patients away from OGD assessment, especially for low-yield symptoms such as reflux.

However, these measures do not address the core issue with current gastroscopy provision in the UK, which is the weak association between most upper GI symptoms and underlying pathology. This is especially true for oesophageal and gastric cancers, where early treatable stages often have no symptoms, and symptoms only appear in later stages (if at all) where diagnosis has little impact on treatment. [37] Ongoing research into circulating DNA obtained via “liquid biopsies” aims to change this by detecting oesophageal and gastric cancers through minimally invasive samples obtained from asymptomatic individuals. [38, 39] If evidence of efficacy in earlier detection of cancer can be established this approach could offer an alternative pathway for diagnosing upper GI cancers, either as a screening tool within the asymptomatic population or as an adjunct to help triage and inform patients with upper GI symptoms.

The automatic, real-time NED uploads allow a vast data repository to be compiled without impacting on endoscopist workload. This, combined with near total UK coverage, [40] makes NED unique and enables novel insights into UK endoscopy. However, despite this being the largest known analysis of UK gastroscopy practice, some sites were not uploading to NED at the time of the study. This raises the potential for bias, as non-uploading sites may have different practices when compared with those uploading. Moreover, even though this analysis included almost 400,000 procedures, the numbers of cancers in some symptom groups and age-groups were relatively small.

Uploads without a recorded diagnosis, which were excluded from analysis, were an issue involving certain endoscopy reporting systems; however, a post hoc sensitivity analysis revealed the indications and PPVs for these systems following exclusions closely resembled other systems which reliably recorded diagnosis, suggesting substantial bias was unlikely.

The limitations of this study include the method of data compilation. Although anonymising the data facilitated the implementation of the NED, it also resulted in the inability to determine whether multiple endoscopies were carried out in the same patients or confirm diagnoses through histological means. This raises the possibility of false -positive and false -negative diagnoses, but although the overall PPVs may be either over or under-estimated it is expected that these limitations would affect all patient groups equally and thus would not significantly impact variations by age-group, patient sex, and indication.

Conclusions

The analysis of a novel national database reveals inefficient use of gastroscopy resources in the UK. Despite a minimal risk of significant pathology, one-third of gastroscopies were performed on patients under 50, and almost 60% were conducted on females, despite males being at higher risk for major pathology, including a threefold increased likelihood of cancer.

This inefficient utilisation extends to the investigation of symptoms, as two-thirds of symptomatic gastroscopies focused on symptoms with the lowest cancer risk: anaemia, reflux, and dyspepsia. Although reflux is a better predictor of BO, its positive predictive value remains low, especially in younger and female patients. By reducing the proportion of gastroscopies for low-yield symptoms and in younger and female patients, valuable capacity could be freed up to promptly investigate higher-risk groups, such as males with dysphagia, while minimising unnecessary procedures for those unlikely to benefit from gastroscopy.

References

1. Ravindran, S., et al., *National census of UK endoscopy services 2021*. Frontline Gastroenterology, 2022: p. flgastro-2022-1.
2. Arnold, M., et al., *Progress in cancer survival, mortality, and incidence in seven high-income countries 1995–2014 (ICBP SURVMARK-2): a population-based study*. The Lancet Oncology, 2019. **20**(11): p. 1493-1505.
3. Arnold, M., et al., *Global Burden of 5 Major Types of Gastrointestinal Cancer*. Gastroenterology., 2020. **159**(1): p. 335-349.e15.
4. Arnold, M., et al., *International variation in oesophageal and gastric cancer survival 2012–2014: differences by histological subtype and stage at diagnosis (an ICBP SURVMARK-2 population-based study)*. Gut, 2022. **71**(8): p. 1532-1543.
5. Miles, A., et al., *Perceived diagnostic delay and cancer-related distress: a cross-sectional study of patients with colorectal cancer*. Psycho-Oncology, 2017. **26**(1): p. 29-36.
6. Rutter, M.D., et al., *Impact of the COVID-19 pandemic on UK endoscopic activity and cancer detection: a National Endoscopy Database Analysis*. Gut, 2020: p. gutjnl-2020-322.
7. Alderwick, H. and A. Charlesworth, *A long term workforce plan for the English NHS*. BMJ :, 2022: p. o1047.
8. *Securing the future workforce supply. Gastrointestinal endoscopy workforce review*. 2017: online.
9. *The National Endoscopy Database (NED)*. 2021 [cited 2021 10th April]; Available from: <https://nedpilot.thejag.org.uk/>.
10. Lee, T.J., et al., *Development of a national automated endoscopy database: The United Kingdom National Endoscopy Database (NED)*. United European Gastroenterology Journal, 2019. **7**(6): p. 798-806.
11. NICE. *NICE guideline [NG12]: Suspected cancer: recognition and referral*. 2015 29/1/2021 [cited 2021 16th Apr]; Available from: <https://www.nice.org.uk/guidance/ng12/chapter/Recommendations-organised-by-symptom-and-findings-of-primary-care-investigations#abdominal-symptoms>.
12. Edwin, B.W., *Probable Inference, the Law of Succession, and Statistical Inference*. Journal of the American Statistical Association. **22**(158): p. 209-212 , year = 1927.
13. H., B. and P. R., *Applied Mixed Models in Medicine* , in *Statistics in Practice*. 2006, West Sussex UK: John Wiley & Sons.
14. Rasmussen, S., et al., *Predictive values of upper gastrointestinal cancer alarm symptoms in the general population: a nationwide cohort study*. BMC Cancer, 2018. **18**(1).
15. Numans, M.E., et al., *How Useful is Selection Based on Alarm Symptoms in Requesting Gastroscopy? An Evaluation of Diagnostic Determinants for Gastro-oesophageal Malignancy*. Scandinavian journal of gastroenterology., 2001. **36**(4): p. 437-443.
16. Hungin, A.P., et al., *What happens to patients following open access gastroscopy? An outcome study from general practice*. The British journal of general practice :, 1994. **44**(388): p. 519-521.
17. Lambert, R., *Digestive endoscopy: relevance of negative findings*. 1999. **31**(8): p. 761-772.
18. Drummond, F.J., et al., *Factors prompting PSA-testing of asymptomatic men in a country with no guidelines: a national survey of general practitioners*. BMC Family Practice, 2009. **10**(1): p. 3.
19. Ravindran, S., et al., *National census of UK endoscopy services in 2019*. Frontline Gastroenterol, 2021. **12**(6): p. 451-460.
20. Pritchard, D.M., et al., *Cost-effectiveness modelling of use of urea breath test for the management of *Helicobacter pylori*-related dyspepsia and peptic ulcer in the UK*. BMJ Open Gastroenterology, 2021. **8**(1): p. e000685.
21. Lansdorp-Vogelaar, I. and L. Sharp, *Cost-effectiveness of screening and treating *Helicobacter pylori* for gastric cancer prevention*. Best Practice & Research Clinical Gastroenterology, 2013. **27**(6): p. 933-947.

22. Gisbert, J.P. and X. Calvet, *Helicobacter Pylori "Test-and-Treat" Strategy for Management of Dyspepsia: A Comprehensive Review*. Clinical and translational gastroenterology., 2013. **4**(3): p. e32.
23. Elwyn, G., et al., *Influencing referral practice using feedback of adherence to NICE guidelines: a quality improvement report for dyspepsia*. Quality and Safety in Health Care, 2007. **16**(1): p. 67-70.
24. Kamran, U., et al., *Assessment of the role of the Edinburgh dysphagia score in referral triage in a national service evaluation of the urgent suspected upper gastrointestinal cancer pathway*. Alimentary Pharmacology & Therapeutics, 2022. **55**(9): p. 1160-1168.
25. O'Sullivan, J.W., et al., *Overtesting and undertesting in primary care: a systematic review and meta-analysis*. BMJ Open, 2018. **8**(2): p. e018557.
26. Ching, H.-L., et al., *Reassessing the value of gastroscopy for the investigation of dyspepsia*. Frontline Gastroenterology, 2018. **9**(1): p. 62-66.
27. NICE *Dyspepsia and gastro-oesophageal reflux disease in adults*. 2015. [QS96].
28. Stanghellini, V., et al., *Gastroduodenal Disorders*. Gastroenterology., 2016. **150**(6): p. 1380-1392.
29. Chadwick, G., et al., *A population-based, retrospective, cohort study of esophageal cancer missed at endoscopy*. Endoscopy, 2014. **46**(7): p. 553-60.
30. Runge, T.M., J.A. Abrams, and N.J. Shaheen, *Epidemiology of Barrett's Esophagus and Esophageal Adenocarcinoma*. Gastroenterology Clinics of North America, 2015. **44**(2): p. 203-231.
31. van Blankenstein, M., et al., *Age and Sex Distribution of the Prevalence of Barrett's Esophagus Found in a Primary Referral Endoscopy Center*. The American journal of gastroenterology., 2005. **100**(3): p. 568-576.
32. Bhat, S.K., et al., *Oesophageal adenocarcinoma and prior diagnosis of Barrett's oesophagus: a population-based study*. Gut, 2015. **64**(1): p. 20-5.
33. Pilonis, N.D., et al., *Use of a Cytosponge biomarker panel to prioritise endoscopic Barrett's oesophagus surveillance: a cross-sectional study followed by a real-world prospective pilot*. The Lancet Oncology, 2022. **23**(2): p. 270-278.
34. Januszewicz, W., et al., *Safety and Acceptability of Esophageal Cytosponge Cell Collection Device in a Pooled Analysis of Data From Individual Patients*. Clinical Gastroenterology and Hepatology, 2019. **17**(4): p. 647-656.e1.
35. Neilson, L.J., et al., *Measuring patient experience of Cytosponge using the Newcastle ENDOPREM*. Frontline gastroenterology., 2022: p. flgastro-2022-102288.
36. Di Pietro, M., et al., *Use of Cytosponge as a triaging tool to upper gastrointestinal endoscopy during the COVID-19 pandemic*. The Lancet Gastroenterology & Hepatology, 2020. **5**(9): p. 805-806.
37. Boulton-Jones, J.R., M.C. Follows, and A.A. Mahmoud, *Open-Access Endoscopy: Are Age-Based Guidelines Justified? An Audit of Experience of 1000 Open-Access Endoscopies at a District General Hospital*. Endoscopy., 2003. **35**(1): p. 68-73.
38. Lengyel, C.G., et al., *The Emerging Role of Liquid Biopsy in Gastric Cancer*. Journal of Clinical Medicine, 2021. **10**(10): p. 2108.
39. Yuan, Z., et al., *Liquid biopsy for esophageal cancer: Is detection of circulating cell-free DNA as a biomarker feasible?* Cancer Communications, 2021. **41**(1): p. 3-15.
40. Beaton, D., et al., *UK endoscopy workload and workforce patterns: is there potential to increase capacity? A BSG analysis of the National Endoscopy Database*. Frontline Gastroenterology, 2022: p. flgastro-2022-1.