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Original Research

An evaluation of the epidemiology, management and outcomes for perforated peptic ulcers across the North of England over 15 years: A retrospective cohort study

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ABSTRACT

Background: The management of perforated peptic ulcers has evolved over time and includes laparoscopic or open repair, and conservative management. The utilisation of, and outcomes from these strategies are not clear. Trends in epidemiology, management and outcomes for perforated peptic ulcer across the North of England over a 15-year period were analyzed.

Patients and Methods: Emergency General Surgical admissions data from nine NHS trusts in the North of England from 2002 to 2016 were collected and analyzed, including demographics, interventions and outcomes. Cases were identified using ICD-10 codes K25, K26 and K27 0.1, 0.2, 0.5, 0.6.

Results: Peptic ulcer perforation accounted for 2373 of 491141 admissions (0.48%), with a decreased incidence over time (0.62% in 2002–2006 to 0.36% in 2012–2016). Over the 15 years studied, an increasing proportion of cases were managed laparoscopically (4.5%–18.4%, $p < 0.001$) and under upper-gastrointestinal consultants (15.4%–28.6%, $p < 0.001$). Thirty-day inpatient mortality improved significantly over time (20.0%–10.8%, $p < 0.001$) as did mean length of stay (17.3–13.0 days, $p = 0.001$). Independent predictors of increased 30-day mortality were increasing age, Charlson co-morbidity score, clinical and operative risk, earlier year of admission, winter admission, weekend/bank holiday procedure and management strategy, with laparotomy and conservative management increasing risk.

Conclusion: Outcomes (30-day mortality and LOS) improved significantly over the study period. Laparoscopic approach was increasingly utilised and was an independently significant factor associated with improved mortality. Management by upper-gastrointestinal specialists increased rates of laparoscopy, with fewer conversions to open.

1. Introduction

The management of peptic ulcers has been revolutionised in recent decades by the introduction of proton pump inhibitors (PPIs) and eradication therapy for *Helicobacter pylori* [1,2]. Recurrence of peptic ulcers with eradication is 6% compared to 67% without and 4% vs 59% for gastric ulcers [3]. However, the resulting decrease in incidence of peptic ulcers has not been matched by a decrease in incidence of perforated peptic ulcers (PPUs) which has remained stable, occurring in 2–10% of all patients with peptic ulcer disease [4,5]. PPU carries a significant mortality of 10–40%, with increasing age, presence of co-morbidities, diagnostic and treatment delay and perioperative shock being factors associated with poor outcomes [6–9].

Primary open repair with pedicled omental patch remains the mainstay of treatment, although a laparoscopic approach, first described in 1990 [10], has also been widely adopted [11]. Various studies including randomised controlled trials and subsequent meta-analyses [6,7,12–19] have compared the two; similar morbidity and mortality were observed, with shorter in-hospital stay and less post-operative pain in patients who underwent laparoscopic repair. A number of recent clinical guidelines have noted the benefits of laparoscopy but do not recommend one technique over the other [20–22]. Laparoscopic techniques are reportedly now used in 32%–40% with a conversion to open rate of 12–25% [7,11].

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Table 1
Data fields requested from the National Health Service Foundation Trusts' Caldicott Guardian.

Demographic fields	Age, gender, postcode
Co-morbidity fields	ICD-10 diagnoses (excluding primary diagnosis)
Diagnosis/operation fields	Primary diagnosis (ICD-10 diagnosis 1), operation date, operation type (OPCS codes for operation 1 onwards)
Outcome fields	Admission date and source, discharge date and location, readmission within 30 days of discharge, mortality, date of death

Conservative management has been shown to carry acceptable morbidity and mortality in selected cases, or those unsuitable for surgery [23–25]. Although management of perforated *gastric* ulcer is complicated by the need to consider malignancy, initial management is usually with patch repair and biopsy. Primary resection is rare [26].

The aims of this study were to describe the epidemiology of PPU, the associated management strategies, and to assess the factors associated with any additional mortality risk in patients admitted with PPU to National Health Service (NHS) hospitals in the North of England during a 15-year interval.

2. Methods

Details of every admission, accident and emergency attendance and outpatient appointment in NHS hospitals are submitted to the Health and Social Care Information Centre and compiled into Hospital Episode Statistics (HES) [26]. Data from all acute NHS Foundation Trusts in the North of England over a 15-year period from January 1st, 2002 to December 31st, 2016 were collected, specifically data fields listed in Table 1. These data were sought from all acute NHS Foundation Trusts in the North of England after Caldicott approval in the Trust.

2.1. Data definitions

The cohort comprised all patients aged 16 or above admitted as an emergency under a general surgeon in the North of England between 2002 and 2016 with a diagnosis of perforated peptic ulcer using International Statistical Classification of Diseases and Related Health Problems (ICD)-10 codes: K25 (gastric ulcer), K26 (duodenal ulcer), and K27 (peptic ulcer, site unspecified), with perforation codes: 0.1 (acute with perforation), 0.2 (acute with both haemorrhage and perforation), 0.5 (chronic with perforation), 0.6 (chronic with both haemorrhage and perforation) [27].

Postal codes were converted to Index of Multiple Deprivation (IMD) scores and deprivation quintiles [28,29]. Co-morbidity data (secondary ICD-10 diagnostic codes) were converted to Charlson scores [30,31] using weightings employed by the hospital standardized mortality ratio [32,33]. Primary and secondary procedure data, provided by hospital Trusts, were used to identify which patients underwent surgical intervention for peptic ulcer perforation after admission (excluding endoscopic or radiological procedures). This was used to assign cases to management strategy groups: conservative management, open surgery, laparoscopic and laparoscopic converted to open. The relevant OPCS Classification of Surgical Operations and Procedures codes are as follows: G35.1, G35.2, G35.8, G36.2, G36.3, G36.8, G36.9, G38.8, G38.9, G52.1, G52.2, G52.3, G52.8 and G52.9. For laparoscopic approach, code Y75.2 was added (or Y50.8 in OPCS v4.2 or earlier). For laparoscopic converted to open, code Y71.4 (or Y71.8 in OPCS v4.2 or earlier) [34]. Conservatively managed patients were identified from patients not undergoing relevant abdominal operative procedures.

The data provided enabled calculation of gender, age at admission, day of admission and operation, source of admission (e.g. Emergency Department or Primary Care), season of admission, trust size (small/medium: under 458 beds; large/very large: over 458 beds), hospital consultant sub-specialty, operative and clinical risk group. To partially account for patients' clinical profile, clinical and operative risk categories were derived by ranking diagnoses and procedures into three equally sized groups based on crude 30-day mortality for the principle recorded diagnosis and surgical procedures, respectively. Consultant subspecialty was mapped from the consultant who was responsible for the hospital episode to the respective subspecialty register. The mortality outcome of interest was in-hospital death within 30 days of procedure (for operatively managed patients) or admission (for conservatively managed patients). Secondary outcomes were in-hospital death within 90 days, duration of hospital stay (LOS), time to operation, days to discharge from procedure and conversion to open (in laparoscopically managed cases).

2.2. Statistical analysis

These retrospective observational data were analyzed according to three 5-year cohorts: 1 January 2002 to 31 December 2006; 1 January 2007 to 31 December 2011; and 1 January 2012 to 31 December 2016. Categorical data were summarized using frequencies and percentages, and continuous data using the mean with its 95% confidence interval. Changes in case mix over time were tested using Pearson's $\chi 2$ test for trend for categorical variables, and differences between continuous variables were analyzed using ANOVA with post hoc testing.

Factors associated with 30-day in-hospital mortality were determined using a Cox regression with time-dependent co-variates to describe the hazards associated with 30-day in hospital mortality. Factors with $p < 0.20$ in the univariate models were tested in multivariate models with forward stepwise regression including variables $p < 0.050$ with significant improvement of model fit (reduction in Akaike's information criterion of at least 4). Case mix factors included in the models were: age group, Charlson co-morbidity score (grouped 0–1, 2–4, or ≥5), gender, year of admission (in 5-year cohorts), season of admission, deprivation quintile, admission source, clinical risk group, operative risk group, consultant subspecialty, admitting trust size, weekend/weekday admission, weekend/weekday procedure, and management strategy (all categorical).

Data were collected in Excel® 2016 (Microsoft, Redmond, Washington, USA) and analyses were undertaken using SPSS® version 23.0 (IBM Corp, 2015). Statistical significance was defined as $p < 0.05$. This work has been reported in line with the STROCSS criteria [36].

3. Results

3.1. Patient characteristics: changes over study period

Over 15 years, 2,373 patients were admitted with PPU (0.48% of all 491,141 General Surgical admissions) in the North of England (Table 2). There was a significant reduction in the incidence of PPU over the study period, with 981 (0.62%) admissions in 2002–2006 and 576 (0.36%) in 2012–2016 ($p < 0.001$).

The mean age was 59.3 years, and the majority were male (54.3%). There was a significant trend of decreasing mean age of these patients from 61.1 years (in 2002–2006) to 57.2 years (in 2012–2016, $p < 0.001$). Levels of comorbidity did not vary significantly, over time ($p = 0.060$). There was significant variation in clinical risk groups, which acted as a surrogate for illness severity, over time, with fewer patients in the highest and lowest risk groups over time ($p < 0.001$).

A significant rise in admissions from the Emergency Department was noted (rising from 67.7% in 2002–2006 to 87.0% in 2012–2016), with a corresponding reduction in admissions from Primary Care

Table 2
Baseline characteristics for patients admitted with perforated duodenal ulcer, by study period.

	Study Year Period				
	2002–2006	2007–2011	2012–2016	Overall	*P*†
Total general surgery admissions	159106	170970	161065	491141	
PPU Admissions	981 (0.62)	816 (0.48)	576 (0.36)	2373 (0.48)	
*Mean Age**	61.1 (59.9–62.3)	58.5 (57.2–59.8)	57.2 (55.7–58.8)	59.3 (58.5–60.0)	< **0.001**
Age group					< **0.001**
16-29	74 (7.6)	72 (8.9)	39 (6.8)	185 (7.9)	
30-39	82 (8.4)	75 (9.3)	72 (12.6)	229 (9.7)	
40-49	117 (11.9)	100 (12.4)	94 (16.5)	311 (13.2)	
50-59	144 (14.7)	130 (16.1)	91 (15.9)	365 (15.5)	
60-69	156 (15.9)	142 (17.6)	108 (18.9)	406 (17.2)	
70-79	238 (24.3)	163 (20.2)	80 (14.0)	481 (20.4)	
80-89	146 (14.9)	112 (13.9)	73 (12.8)	331 (14.0	
≥90	23 (2.3)	11 (1.4)	14 (2.5)	48 (2.0)	
Gender					0.167
Female	448 (45.7)	353 (43.3)	235 (40.8)	1036 (43.7)	
Male	533 (54.3)	463 (56.7)	341 (59.2)	1337 (56.3)	
Charlson Score					0.060
0-1	666 (67.9)	516 (63.2)	351 (60.9)	1533 (64.6)	
2–4	279 (28.4)	262 (32.1)	200 (34.7)	741 (31.2)	
≥ 5	36 (3.7)	38 (4.7)	25 (4.3)	99 (4.2)	
Clinical Risk Group					< **0.001**
1 (lowest)	311 (31.7)	256 (31.4)	158 (27.4)	725 (30.6)	
2	513 (52.3)	466 (57.1)	364 (63.2)	1343 (56.6)	
3 (highest)	157 (16.0)	94 (11.5)	54 (9.4)	305 (12.9)	
Deprivation Score					0.747
1 (most)	264 (32.8)	242 (35.7)	150 (31.8)	656 (33.6)	
2	189 (23.5)	166 (24.5)	108 (22.9)	463 (23.7)	
3	143 (17.8)	114 (16.8)	81 (17.2)	338 (17.3)	
4	93 (11.6)	70 (10.3)	61 (12.9)	224 (11.5)	
5 (least)	115 (14.3)	86 (12.7)	72 (15.3)	173 (14.0)	
Trust Size					0.481
Small/Medium	474 (48.3)	377 (46.2)	284 (49.3)	1134 (47.8)	
Large/Very Large	507 (51.7))	439 (53.8)	292 (50.7)	1238 (52.2)	
Season					0.817
Spring	258 (26.3)	217 (26.6)	152 (16.4)	627 (26.4)	
Summer	252 (25.7)	200 (24.5)	156 (27.1)	608 (25.6)	
Autumn	253 (25.8)	204 (25.0)	131 (22.7)	588 (24.8)	
Winter	218 (22.2)	195 (23.9)	137 (13.8)	550 (23.2)	
Admission Method					< **0.001**
ED	664 (67.7)	660 (80.9)	481 (87.0)	1805 (76.8)	
PC	226 (23.0)	105 (12.9)	36 (6.5)	367 (15.6)	
Consultant Clinic	4 (0.4)	2 (0.2)	3 (0.5)	9 (0.4)	
Other	87 (8.9)	49 (6.0)	33 (6.0)	169 (7.2)	
Admitting Subspecialty					< **0.001**
UGI	151 (15.4)	172 (21.1)	165 (28.6)	448 (20.6)	
Non-UGI	830 (84.6)	644 (78.9)	411 (71.4)	1885 (79.4)	
Admission Day of Week					0.476
Weekday	701 (71.5)	585 (71.7)	397 (68.9)	1683 (70.9)	
Weekend	280 (28.5)	231 (28.3)	179 (31.1)	690 (29.1)	
Procedure Day of Week					0.421
Weekday	541 (72.6)	421 (70.8)	290 (69.0)	1252 (71.1)	
Weekend	204 (27.4)	174 (29.2)	130 (31.0)	508 (28.9)	
Operative Risk Group					< **0.001**
1 (lowest)	0 (0)	1 (0.1)	0 (0)	1 (0.0)	
2	0 (0)	0 (0)	0 (0)	0 (0)	
3	49 (5.6)	92 (12.6)	78 (15.4)	219 (10.4)	
4 (highest)	821 (94.4)	636 (87.2)	429 (84.6)	1886 (89.6)	
Management Strategy					< **0.001**
Laparoscopic	44 (4.5)	79 (9.7)	106 (18.4)	229 (9.7)	
Converted to open	2 (0.2)	27 (3.3)	26 (4.5)	55 (2.3)	
Laparotomy	824 (84.0)	623 (76.3)	375 (65.1)	1822 (76.8)	
Conservative	111 (11.3)	87 (10.7)	69 (12.0)	267 (11.3)	

Values in parentheses are percentages unless indicated otherwise; *values are mean (95% c.i.). Percentages and proportions were derived by excluding missing data from the variable. †$\chi 2$ test for difference, except ‡ANOVA.(PDU, perforated duodenal ulcer; ED, emergency department; PC, primary care; UGI, upper gastrointestinal surgeon.)

(dropping from 23.0% in 2002–2006 to 6.5% in 2012–2016, $p < 0.001$).

An increasing proportion of patients were admitted under UGI consultants from 15.4% in 2002–2006 to 28.6% in 2012–2016 ($p < 0.001$). Laparoscopic techniques were employed more over time, from 4.5% in 2002–2006 to 18.4% in 2012–2016. There was a corresponding drop in patients managed by laparotomy from 84.0% to 65.1% ($p < 0.001$). The proportion of patients managed conservatively did not change significantly over time: 10.5% in 2002–2006 to 12.0% in 2012–2016.

Table 3
Trends in patient outcomes over time, including 30-day crude mortality by management strategy.

	Study Year Period				
	2002–2006	2007–2011	2012–2016	Overall	*P*†
*Length of Stay (Days)**	17.3 (15.9–18.8)	16.3 (14.6–18.1)	13.0(11.7–14.2)	15.9 (15.0–16.8)	**0.001**
*Time to Procedure (Days)**	2.1 (1.5–2.7)	2.6 (1.8–3.4)	1.5 (1.1–2.0)	2.1 (1.8–2.5)	0.091
*Time to Discharge Postoperatively (Days)**	15.8 (14.3–17.3)	13.3 (11.5–15.1)	11.0 (9.8–12.2)	13.7 (12.8–14.6)	< **0.001**
30-Day *Mortality*	196 (20.0)	114 (14.1)	62 (10.8)	372 (15.7)	< **0.001**
- Laparoscopic	3 (6.8)	2 (2.5)	4 (3.8)	9 (3.9)	0.500
- Converted to Open	0 (0)	0 (0)	3 (11.5)	3 (5.5)	0.170
- Laparotomy	147 (17.9)	92 (14.9)	43 (11.5)	282 (15.5)	**0.016**
- Conservative	46 (41.8)	20 (23.0)	12 (17.4)	78 (19.3)	**0.001**
90-Day *Mortality*	211 (21.6)	124 (15.3)	74 (12.8)	409 (17.3)	< **0.001**

Values in parenthesis are percentages unless indicated otherwise. *values displayed are mean (95% c.i).
Percentages and proportions were derived by excluding missing data from the variable. †$\chi 2$ test for difference, except ‡ANOVA.

No significant change in proportion of admissions or procedures occurring over the weekend was observed.

3.2. Patient outcomes: changes over study period

Mean overall hospital length of stay decreased significantly over the study period from 17.3 days in 2002–2006 to 13.0 days in 2012–2016 ($p = 0.001$, Table 3), which was largely driven by a significant reduction in postoperative length of stay (15.8 days–11.0 days, $p < 0.001$). No significant difference in mean days-to-procedure was observed.

Thirty day inpatient mortality almost halved over the study period, from 20.0% in 2002–2006 to 10.8% in 2012–2016 ($p < 0.001$), with a similar reduction in 90-day mortality from 21.6% to 12.8% ($p < 0.001$). This trend was observed for those undergoing both laparotomy (17.9%–11.5%, $p = 0.016$), and conservative management (41.8%–17.4%, $p = 0.001$) (Fig. 1).

3.3. Patient characteristics: difference between management strategies

There were significant variations in demographics between management strategies (Table 4). The conservative management group had the greatest mean age (67.8 years), and level of comorbidity compared to the other strategies, with over 50% of patients having multiple co-morbidities (Charlson score ≥ 2, $p < 0.001$).

Meanwhile, laparoscopic and laparoscopic converted to open cases had the youngest cohort of patients with low comorbidity ($p < 0.001$).

Compared to larger Trusts (over 458 beds), there was a significant trend towards laparoscopic management at smaller Trusts and away from conservative management ($p < 0.001$). Admissions under an upper gastrointestinal surgeon were more likely to be managed laparoscopically, accounting for 20.6% of admissions but 45.9% of laparoscopic cases ($p < 0.001$). The conversion-to-open rate under upper gastrointestinal consultants was half the rate under other specialists (11.8% vs 24.8%, $p = 0.006$).

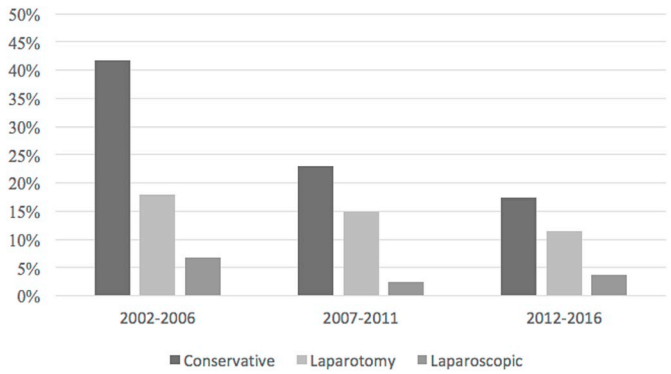

Fig. 1. Changes in 30-day mortality for patients admitted with perforated duodenal ulcers, by management strategy over time.

There was no significant variation between management strategy with regards to gender, season of admission, weekend admission or weekend procedure.

3.4. Outcomes: difference between management strategies

Mean overall length of stay varied significantly by operation type (Table 5), being greatest in the conservative management group (16.9 days) then laparotomy (16.6 days), then laparoscopic converted to open (13.0 days) and least in the laparoscopic group (10.3 days, $p = 0.001$).

Thirty-day inpatient mortality was greatest in the conservative management group (29.3%) then laparotomy (15.5%), converted to open (5.3%) and least in laparoscopically managed patients (3.9%, $p < 0.001$). A similar pattern was observed in 90-day mortality ($p < 0.001$).

There was no significant difference in 30-day mortality between upper gastrointestinal and non-upper gastrointestinal surgeons, regardless of management strategy.

3.5. Predictors of 30-day mortality in patients admitted with perforated peptic ulcers

The multivariate Cox regression analysis (Table 6) identified increasing age, increased Charlson co-morbidity score, earlier year of admission, winter admission, higher clinical and operative risk groups, Weekend/bank holiday procedure (though not weekend/bank holiday admission) and management strategy as independently predictive factors of 30-day mortality. Similar 30-day survival for laparoscopic and converted to open cases, was observed, with laparotomy and conservative management having significantly lower 30-day survival following PPU: Compared to laparoscopic surgery: converted to open adjusted hazard ratio (HR) 1.08 (0.23–5.02, $p = 0.924$), laparotomy HR 2.23 (1.14–4.37) $p = 0.020$) and conservative HR 3.39 (1.68–6.86, $p = 0.001$).

4. Discussion

This study found a decreasing incidence of PPU over the 15 years, from 0.62% of admissions in 2002-06 to 0.36% in 2012-16, which is consistent with other reports in the literature [23]. Noticeably, there was a trend towards younger age at presentation and a greater number of males. This is perhaps an unexpected finding given the proportion of females with PPU in the national and international population appears to be rising and there has been a suggestion that patients with PPU are presenting at increasing age [23,35,36]. Another striking finding from this study was the increasing use of laparoscopy in managing patients. This was accompanied by a significant improvement in outcomes.

Table 4
Baseline characteristics for patients admitted with perforated duodenal ulcer, by management strategy.

	Management Strategy					
	Laparoscopic	Converted to Open	Laparotomy	Conservative	Overall	*P*†
Total	229	55	1822	267	2373	
Mean Age	52.7 (50.1–55.2)	50.8 (45.6–55.9)	59.1 (58.2–60.0)	67.8 (65.8–69.8)	59.3 (58.5–60.0)	< **0.001**
Age group						< **0.001**
16-29	29 (12.7)	8 (14.8)	142 (7.9)	6 (2.2)	185 (7.9)	
30-39	36 (15.8)	9 (16.7)	172 (9.5)	12 (4.5)	229 (9.7)	
40-49	40 (17.5)	9 (16.7)	239 (13.2)	23 (8.6)	311 (13.2)	
50-59	37 (16.2)	8 (14.8)	284 (15.7)	36 (13.5)	365 (15.5)	
60-69	30 (13.2)	10 (18.5)	323 (17.9)	43 (16.1)	406 (17.2)	
70-79	30 (13.2)	6 (11.1)	372 (20.6)	73 (27.3)	481 (20.4)	
80-89	24 (10.5)	4 (7.4)	242 (13.4)	61 (22.8)	331 (14.0)	
≥90	2 (0.9)	0 (0.0)	33 (1.8)	13 (4.9)	48 (2.0)	
Gender						**0.037**
Female	91 (39.7)	19 (34.5)	791 (43.4)	135 (50.6)	1036 (43.7)	
Male	138 (60.3)	36 (65.5)	1031 (56.6)	132 (49.4)	1337 (56.3)	
Charlson Score						< **0.001**
0-1	174 (76.0)	38 (69.1)	1192 (65.4)	129 (48.3)	1533 (64.6)	
2–4	52 (22.7)	15 (27.3)	552 (30.3)	122 (45.7)	741 (31.2)	
≥ 5	3 (1.2)	2 (3.6)	78 (4.3)	16 (6.0)	99 (4.2)	
Clinical Risk Group						< **0.001**
1 (lowest)	62 (27.1)	16 (29.1)	575 (31.6)	72 (27.0)	725 (30.6)	
2	157 (68.6)	32 (58.2)	1018 (55.9)	136 (50.9)	1343 (56.6)	
3 (highest)	10 (4.4)	7 (12.7)	229 (12.6)	59 (22.1)	305 (12.9)	
Deprivation Score						0.403
1 (most)	83 (39.0)	22 (43.1)	498 (33.0)	53 (29.1)	656 (33.6)	
2	49 (23.0)	10 (19.6)	364 (24.1)	40 (22.0)	463 (23.7)	
3	28 (13.1)	5 (9.8)	271 (18.0)	34 (18.7)	338 (17.3)	
4	23 (10.8)	6 (11.8)	167 (11.1)	28 (15.4)	224 (11.5)	
5 (least)	30 (14.1)	8 (15.8)	208 (13.8)	27 (14.8)	273 (14.0)	
Trust Size						< **0.001**
Small/Medium	137 (59.8)	34 (61.8)	852 (46.8)	112 (41.9)	1135 (47.8)	
Large/Very Large	92 (40.2)	21 (38.2)	970 (53.2)	155 (58.1)	1238 (52.2)	
Season						0.079
Spring	59 (25.8)	19 (34.5)	470 (25.8)	79 (29.6)	627 (26.4)	
Summer	61 (26.6)	19 (34.5)	457 (25.1)	71 (26.6)	608 (25.6)	
Autumn	68 (29.7)	7 (12.7)	453 (24.9)	60 (22.5)	588 (24.8)	
Winter	41 (17.9)	10 (18.2)	442 (24.3)	57 (21.3)	550 (23.2)	
Admission Method						< **0.001**
ED	201 (89.3)	47 (87.0)	1352 (74.9)	205 (76.8)	1805 (76.8)	
PC	17 (7.6)	4 (7.4)	312 (17.3)	34 (12.7)	367 (15.6)	
Consultant Clinic	1 (0.4)	0 (0.0)	7 (0.4)	1 (0.4)	9 (0.4)	
Other	6 (2.7)	3 (5.6)	133 (7.4)	27 (10.1)	169 (7.2)	
Admitting Subspecialty						< **0.001**
UGI	105 (45.9)	14 (25.5)	315 (17.3)	54 (20.2)	488 (20.6)	
Non-UGI	124 (54.1)	41 (74.5)	1507 (82.7)	213 (79.8)	1885 (79.4)	
Admission Day of Week						0.099
Weekday	162 (70.7)	41 (74.5)	1274 (69.9)	206 (77.2)	1683 (70.9)	
Weekend	67 (29.3)	14 (25.5)	548 (30.1)	61 (22.8)	690 (29.1)	
Procedure Day of Week						0.643
Weekday	147 (70.7)	40 (76.9)	1065 (71.0)	–	1252 (71.1)	
Weekend	61 (29.3)	12 (23.1)	435 (29.0)	–	608 (28.9)	
Operative Risk Group						< **0.001**
1 (lowest)	0 (0)	0 (0.0)	1 (0.1)	–	1 (0.0)	
2	0 (0)	0 (0.0)	0 (0.0)	–	0 (0.0)	
3	6 (2.6)	1 (1.8)	212 (11.6)	–	219 (10.4)	
4 (highest)	223 (97.4)	54 (98.2)	1609 (88.3)	–	1886 (89.6)	

Values in parentheses are percentages unless indicated otherwise; *values are mean (95% c.i.). Percentages and proportions were derived by excluding missing data from the variable. ED, emergency department; PC, primary care; UGI, upper gastrointestinal surgeon. †$\chi 2$ test for difference, except ‡ANOVA.

Given these positive outcomes and the growing body of evidence supporting laparoscopic management, it is perhaps surprising that conservative management was more common that laparoscopic, even in our most recent cohort.

Within the earliest cohort analyzed, open surgical repair was the most common strategy employed. Over time more cases were managed with a laparoscopic approach (4.5% initially to 18.4% in the final cohort) however this fell short of other published rates (30%) [11]. On closer inspection, cases admitted under upper gastrointestinal specialists achieve laparoscopy rates of 21.5% compared to 6.6% amongst other surgeons. The observed overall 30-day mortality rates, 3.9% for laparoscopic (5.5% when converted to open), 15.5% for laparotomy and 29.3% for conservative management also corresponded well with published rates which range between 3.6 and 10% for laparoscopy and 6–30% overall [12,15,37]. The conversion to open rate of 19.4% was also similar to other published rates (12–25%) [6,7,11,15], although amongst upper gastrointestinal surgeons, there was a significantly lower rate of 11.8%. Increasing conversion rate, over time, from 8.7% to 19.7% may relate to increased confidence amongst surgeons to attempt laparoscopic approach in a less selective group of patients, whilst accepting potential conversion to open as the default position.

The increasing use of laparoscopy may be due to a greater number

Table 5
Outcomes for patients admitted with perforated duodenal ulcer, by management strategy.

	Management Strategy					
	Laparoscopic	Converted to Open	Laparotomy	Conservative	Overall	*P*†
*Length of Stay (Days)**	10.3 (8.2–12.3)	13.0 (8.5–17.4)	16.6 (15.5–17.7)	16.9 (14.2–19.6)	15.9 (15.0–16.8)	**0.001**
*Time to Procedure (Days)**	1.0 (0.1–1.9)	0.6 (0.3–0.8)	2.3 (1.9–2.7)	N/A	2.1 (1.8–2.5)	**0.038**
*Time to Discharge Postoperatively (Days)**	9.6 (7.7–11.5)	12.7 (8.1–17.3)	14.3 (13.2–15.3)	N/A	13.7 (12.8–14.6)	**0.009**
30-Day *Mortality*	9 (3.9)	3 (5.5)	282 (15.5)	78 (29.3)	372 (15.7)	< **0.001**
UGI 30-Day *Mortality*	4 (3.8)	1 (7.1)	48 (15.2)	13 (24.1)	66 (13.5)	**0.002**
Non-UGI 30-Day *Mortality*	5 (4.0)	2 (4.9)	234 (15.6)	65 (30.7)	306 (16.3)	< **0.001**
90-Day *Mortality*	11 (4.8)	4 (7.3)	310 (17.1)	84 (31.6)	409 (17.3)	< **0.001**

Values in parenthesis are percentages unless indicated otherwise. *values displayed are mean (95% c.i).
Percentages and proportions were derived by excluding missing data from the variable. †$\chi 2$ test for difference, except ‡ANOVA.

of surgeons being proficient with laparoscopic techniques and using them within their elective practice. There is increasing evidence that outcomes for laparoscopic intervention are comparable or superior to open intervention in many cases with shorter in-hospital stay, less post-operative pain and post-operative analgesia requirements [6,7,12–19,38]. Indeed, within this population it was observed that laparoscopically managed cases had a significantly shorter LOS and 30-day mortality rate, and was an independent predictor of lower mortality compared to other management strategies (Table 6). Interestingly, these improved outcomes were also observed in cases when a laparoscopic approach was converted to open. It should be noted, however, that laparoscopic management was associated with significantly younger patients and lower comorbidity levels. This may indicate that case selection has played a role in our observed laparoscopic outcomes. There may be a number of barriers to further adoption of laparoscopic techniques including unavailability of surgeons experienced in laparoscopic surgery, as well as perceptions amongst surgeons that open repair is a more familiar and faster procedure [14]. These may explain why the proportion of laparoscopically managed cases is not higher than 20% in the most recent cohort.

Thirty-day mortality and LOS were significantly higher for those managed conservatively. These patients tended to be older with a greater number of co-morbidities than those undergoing surgery. An initial period of conservative management has been shown to be a safe alternative to operative intervention in patients *under* 70 years old [24,25], although this has not been adopted as first line management, perhaps because in patients ultimately requiring an operation, treatment delay is associated with worse outcomes [6–9]. One limitation of our analysis is that we were unable to identify cases of failed initial conservative management so all patients who had an operation were included in the surgical intervention groups, regardless of initial treatment strategy. Furthermore, there may have been two distinct cohorts within our “Conservative management” group: fit, stable patients not requiring surgery who are predicted to settle with standard medical management, and those who were too frail for surgery to be appropriate, who were palliated if a trial of conservative treatment appeared to be failing.

Irrespective of management strategy there were significant improvements in LOS and 30-day inpatient mortality over time. The reason for this is likely to be multifactorial. Increasing use of CT to expedite diagnosis [7,39] may play a part although no decrease in “time to procedure” was observed. The majority of deaths in patients with PPU is due to sepsis [7]. The impact of the Surviving Sepsis Campaign [40] will have made clinicians more aware of the importance of timely and appropriate management of sepsis. Other organisational changes to in-patient care provision including MDTs and care bundles [41,42], as well as improved hand-over procedures and early warning scores [43,44] may also have contributed. The institution of enhanced recovery pathways within many specialties elective patient management may have also translated into more aggressive and goal-directed post-operative management for non-elective cases. Similarly the increasing subspecialisation of gastrointestinal surgical services, alongside familiarity with laparoscopic techniques could be considered to contribute to patient outcomes [45,46]. Whilst Cox regression did not identify management by an upper gastrointestinal surgeon as an independently significant factor effecting mortality, the trend of increasing management by upper gastrointestinal teams may have been a factor in improved outcomes.

Of note there was a decreasing trend of patients with perforated peptic ulcers presenting through referral from primary care. This may represent increasing difficulty in accessing primary care services, with a tendency to present directly to the hospital's Emergency Department, or patients appropriately attending hospital directly through emergency services. These factors may also have contributed towards patients being seen by a specialist more rapidly and thus expediting the initiation of treatment.

This study demonstrates a significant improvement in outcomes for patients presenting with PPU. This effect is likely to be multifactorial, and the provision of emergency care, from diagnosis, to surgical strategy, to postoperative care can all potentially be refined in order to ensure the best results. Increasing age, higher levels of co-morbidity and winter admission and weekend/bank holiday procedure were all independently associated with increased mortality. Laparoscopic approach was increasingly employed and was an independently significant factor associated with improved mortality. More cases of PPU were admitted under upper gastrointestinal surgeons over time. This may also have contributed to improving outcomes, indeed, these surgeons were significantly more likely to manage patients laparoscopically and conversion to open rates were significantly lower than other specialists.

Further research into effect of organisational and institutional factors would be valuable in identifying factors responsible for the improved outcomes observed. This should include the effect of centralization and subspecialisation of services.

5. Conclusion

Thirty-day mortality and LOS improved significantly over the study period for all management strategies, both operative and non-operative. A laparoscopic approach is increasingly being utilised and was an independently significant factor associated with improved mortality, although this cohort tended to be younger and had fewer co-morbidities. Management by upper-gastrointestinal specialists increased rates of laparoscopy, with fewer conversions to open. Increased age, co-morbidity, winter admission and weekend operation were independently adverse factors.

Provenance and peer review

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Table 6
Multivariate Cox regression model of the significant factors associated with 30-day mortality in patients admitted with perforated duodenal ulcers.

	Unadjusted		Adjusted	
	HR (95% CI)	*p*-value	HR (95% CI)	*p* value
Age Group				
16-29	1		1	
30-39	0.71 (0.10,5.04)	0.732	0.79 (0.11,5.65)	0.818
40-49	2.06 (0.44,9.53)	0.356	1.54 (0.32,7.45)	0.589
50-59	4.48 (1.06,18.9)	0.041	3.33 (0.78,14.31)	0.105
60-69	6.71 (1.63,27.6)	0.008	4.20 (1.01,17.53)	**0.049**
70-79	9.98 (2.45,40.6)	0.001	5.53 (1.34,22.79)	**0.018**
80-89	17.2 (4.24,69.8)	< 0.001	7.92 (1.92,32.73)	**0.004**
≥90	25.9 (6.06,90.2)	< 0.001	8.67 (1.83,41.21)	**0.007**
Charlson Score				
0-1	1		1	
2-4	2.40 (1.88,3.06)	< 0.001	2.15 (1.59,2.92)	< **0.001**
≥5	5.25 (3.69,7.48)	< 0.001	3.80 (2.41,5.98)	< **0.001**
Gender				
Female	1		1	
Male	0.80 (0.64,0.99)	0.044	1.00 (0.76,1.33)	0.988
Year				
2002-2006	1		1	
2007-2011	0.84 (0.65,1.07)	0.162	0.77 (0.60,0.99)	**0.043**
2012-2016	0.67 (0.49,0.92)	0.012	0.64 (0.47,0.89)	**0.007**
Season				
Spring	1		1	
Summer	1.00 (0.73,1.37)	0.997	0.95 (0.64,1.43)	0.822
Autumn	1.16 (0.84,1.59)	0.373	1.34 (0.91,1.98)	0.142
Winter	1.31 (0.96,1.79)	0.084	1.43 (1.08,2.14)	**0.032**
Deprivation Quintile				
1 (Most)	1			
2	1.02 (0.73,1.43)	0.901		
3	1.01 (0.69,1.46)	0.974		
4	1.03 (0.68,1.57)	0.875		
5 (Least)	1.16 (0.80,1.68)	0.428		
Admission Source				
ED	1		1	
PC	1.53 (1.16,2.00)	0.002	1.24 (0.88,1.73)	0.214
Consultant Clinic	1.48 (0.37,5.96)	0.58	1.45 (0.34,6.11)	0.615
Other	1.00 (0.66,1.53)	0.994	0.94 (0.59,1.52)	0.814
Clinical Risk Group				
1 (Lowest)	1		1	
2	1.39 (1.05,1.84)	0.02	1.54 (1.10,2.15)	**0.012**
3 (Highest)	2.91 (2.13,3.98)	< 0.001	2.43 (1.62,3.62)	< **0.001**
Operative Risk Group				
1 (Lowest)	1		1	
2	2.97 (2.21,3.66)	< 0.001	1.61 (1.11,2.39)	< **0.001**
3 (Highest)	4.56 (3.02,5.88)	< 0.001	2.63 (1.15,6.00)	< **0.001**
Consultant Sub-speciality				
Non-UGI	1		1	
UGI	1.23 (0.98,1.49)	0.063	1.00 (0.70,1.42)	0.993
Trust Size				
Low/Medium	1		1	
Large/Very Large	0.85 (0.68,1.06)	0.16	1.19 (0.89,1.60)	0.235
Admission Date				
Weekday	1			
Weekend/Bank Holiday	1.04 (0.82,1.32)	0.767		
Procedure Date				
Weekday	1		1	
Weekend/Bank Holiday	1.32 (0.99,1.75)	0.057	1.31 (1.04,1.74)	**0.039**
Procedure Type				
Laparoscopic	1		1	
Converted to open	0.78 (0.17,3.61)	0.75	1.08 (0.23,5.02)	0.924
Laparotomy	2.51 (1.29,4.88)	0.007	2.23 (1.14,4.37)	**0.020**
Conservative	4.39 (2.19,8.84)	< 0.001	3.39 (1.68,6.86)	**0.001**

Values in parentheses are 95% confidence intervals. HR, hazard ratio; ED, emergency department; PC, primary care; UGI, upper gastrointestinal surgeon.

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Author contribution

1. Charles HN Johnson: Study design, data analysis, writing.
2. Ross C McLean: Study design, data collection, data analysis, writing.
3. Iain McCallum: Study design, data collection, data analysis, writing.

4. Daniel Perren: Study design, data collection, data analysis, writing.
5. Alexander W Phillips: Study design, data analysis, writing.

Conflicts of interest

None.

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CRediT authorship contribution statement

Charles HN. Johnson: Conceptualization, Methodology, Formal analysis, Writing - original draft, Visualization, Project administration. **Ross C. McLean:** Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing - review & editing, Visualization, Project administration. **Iain McCallum:** Conceptualization, Methodology, Validation, Writing - review & editing, Supervision, Project administration. **Daniel Perren:** Methodology, Software, Validation, Investigation, Data curation, Writing - review & editing. **Alexander W. Phillips:** Conceptualization, Methodology, Validation, Writing - review & editing, Supervision, Project administration.

Appendix A. Supplementary data

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