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Original research

Valvular heart disease

Temporal association between invasive procedures and infective endocarditis

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ABSTRACT

Objective Antibiotic prophylaxis has been recommended for patients at increased risk of infective endocarditis (IE) undergoing specific invasive procedures (IPs) despite a lack of data supporting its use. Therefore, antibiotic prophylaxis recommendations ceased in the mid-2000s for all but those at high IE risk undergoing invasive dental procedures. We aimed to quantify any association between IPs and IE.

Methods All 14731 IE hospital admissions in England between April 2010 and March 2016 were identified from national admissions data, and medical records were searched for IP performed during the 15-month period before IE admission. We compared the incidence of IP during the 3 months immediately before IE admission (case period) with the incidence during the preceding 12 months (control period) to determine whether the odds of developing IE were increased in the 3 months after certain IP.

Results The odds of IE were increased following permanent pacemaker and defibrillator implantation (OR 1.54, 95% CI 1.27 to 1.85, $p<0.001$), extractions/surgical tooth removal (OR 2.14, 95% CI 1.22 to 3.76, $p=0.047$), upper (OR 1.58, 95% CI 1.34 to 1.85, $p<0.001$) and lower gastrointestinal endoscopy (OR 1.66, 95% CI 1.35 to 2.04, $p<0.001$) and bone marrow biopsy (OR 1.76, 95% CI 1.16 to 2.69, $p=0.039$). Using an alternative analysis, bronchoscopy (OR 1.33, 95% CI 1.06 to 1.68, $p=0.049$) and blood transfusions/red cell/plasma exchange (OR 1.2, 95% CI 1.07 to 1.35, $p=0.012$) were also associated with IE.

Conclusions This study identifies a significant association between specific IPs (permanent pacemaker and defibrillator implantation, dental extraction, gastrointestinal endoscopy and bronchoscopy) and subsequent IE that warrants re-evaluation of current antibiotic prophylaxis recommendations to prevent IE in high IE risk individuals.

INTRODUCTION

Infective endocarditis (IE) incidence has increased significantly in the last decade in the UK¹ and the rest of Europe.² Responsible factors could include an ageing population, increased intra-cardiac device use (pacemakers, implantable cardioverter-defibrillators, surgical and transcatheter heart valves), vascular interventions (including haemodialysis), injection drug use, greater IE awareness and access to investigations (especially

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Antibiotic prophylaxis (AP) was recommended before various invasive procedures (IPs) to prevent infective endocarditis (IE), but in the mid-2000s, this practice was stopped (except for invasive dental procedures in those at high risk outside the UK), due to an absence of evidence associating these procedures with IE; in the UK, AP stopped altogether. Since then, there has been a significant increase in IE incidence in the UK and the rest of Europe.

WHAT THIS STUDY ADDS

⇒ This study investigated any temporal association between IPs and subsequent IE in England and identified a significant association with IE following implantation of cardiac pacemakers/defibrillators (CIEDs), dental extractions/surgical tooth removal, upper and lower gastrointestinal endoscopy, and bronchoscopy, all previously recommended for AP.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings provide evidence to warrant a re-evaluation of current AP recommendations for IE prevention in those at high IE-risk, particularly with regard to implantation of CIEDs, gastrointestinal endoscopy, dental extractions (in the UK) and bronchoscopy.

echocardiography), and changes in IE prevention guidelines.¹

IE has devastating consequences, and prevention has been the focus of guidelines. Previous UK, European and US guidelines recommended AP for moderate or high IE risk patients undergoing various invasive procedures (IPs), including invasive-dental procedures (IDPs) (online supplemental appendix table S1). With the possible exception of IDPs, however, there is scant evidence linking IPs to IE or evidence that AP prevents IE.³ This, and concerns about adverse drug reactions and the development of antibiotic resistance, led the American Heart Association (AHA)⁴ and European Society for Cardiology (ESC)⁵ to recommend restricting AP use to IDPs in those at high IE risk and the UK National Institute for Health and Care

Box 1 Cardiac conditions used to classify individuals as being at high or moderate infective endocarditis (IE) risk**High IE risk.**

Previous history of IE.

Presence of prosthetic heart valve (including transcatheter valves).

Prosthetic material used for valve repair (including annuloplasty and transcatheter valve procedures).

Unrepaired cyanotic congenital heart disease.

Congenital heart disease treated with palliative shunts or conduits.

Congenital heart defect repaired with surgical or transcatheter technique using prosthetic material or device (first 6 months postprocedure only).

Moderate IE risk

Rheumatic heart disease.

Non-rheumatic valve disease (including mitral valve prolapse).

Congenital valve anomalies (including aortic stenosis).

Hypertrophic cardiomyopathy.

Notes: adapted from the European Society of Cardiology and American Heart Association guidelines.^{7 8 11 12} More extensive details of all diagnoses and procedures (including relevant ICD-10 diagnosis or OPCS-4 procedure codes) included in the definition of those at high or moderate IE risk are provided in online supplemental tables S2 and S3).

Excellence (NICE) to recommend the complete cessation of AP to prevent IE.⁶

This study aimed to investigate any association between specific IPs and subsequent IE in England using a case-crossover methodology during a period when AP prevention of IE was not recommended.

METHODS**IE admissions and IE risk stratification**

All hospital admissions in England are recorded in the Hospital Episode Statistics (HES) database. With UK National Research Ethics Service approval (17/SC/0371) and Confidentiality Advisory Group approval, this resource was used to identify all IE admissions between 1 April 2010 and 31 March 2016. An admission was defined as a single continuous hospital stay (which could comprise several consultant episodes), where an International Classification of Diseases 10th Revision (ICD-10) primary or secondary diagnosis code I33.0, I33.9, I39.0, I39.1, I39.2, I39.3, I39.4 or I39.8, or a primary diagnosis code I38.X, was used for any consultant episode. Patients discharged alive with a <3 day length of hospital stay or elective admission were excluded.⁷ This study is reported according to Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Each patient's HES record was retrieved from 1 January 2000. To stratify individuals into high, moderate or low/unknown risk of IE (box 1), records were searched for ICD-10 diagnosis or Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures Revision 4 (OPCS-4) procedure codes occurring before IE admission that placed them into these categories based on ESC and AHA guidelines (box 1, online supplemental tables S1 and 2).^{4 5}

New IE admissions were distinguished from readmissions by only accepting IE admissions >180 days apart. Consistent with the guidelines, individuals with congenital heart disease

completely repaired with prosthetic material or a device were considered high-risk for IE for 6 months after the procedure and then considered low risk. Individuals not identified as moderate or high risk were considered at low/unknown risk of IE.

Patient and public involvement

Patients were not directly involved in this study.

Invasive procedures

Each patient's record was searched for OPCS-4 IP codes of interest (online supplemental tables S4 and S5) for each 30-day period over the 15 months before IE admission (ie, between 1 January 2009 and 31 March 2016). IPs of interest were those previously recommended for AP in the 2004 British Cardiac Society and 2006 British Society for Antimicrobial Chemotherapy guidance or identified as associated with an increased risk of IE in a recent Swedish study (online supplemental table S1). To avoid the possibility of reverse causation (procedures being performed as part of the investigation or management of IE), we excluded procedures undertaken during the IE admission. Because some cardiac IPs, for example, coronary artery bypass grafting, may be performed simultaneously with procedures such as valve replacement or repair, we only included them when they occurred alone. Although an association has been reported between dialysis and IE,⁸ the case-crossover methodology is inappropriate for a procedure performed with such regularity, and dialysis was excluded from the study. To ensure we counted the number of individuals exposed to each procedure each month (rather than the number of procedures), we counted the first procedure of each type performed on each individual each month.

Restricting IP data to 1 January 2009 through 31 March 2016, meant all IPs were performed after NICE recommended AP use to prevent IE cease (March 2008)⁶ and before any relaxation of this (April 2016).⁹ Thus, any association between IPs and IE should have been fully exposed.

Case-crossover study**Primary analysis**

Monthly exposure to IPs was quantified over the 15 months before IE-related hospital admissions to determine any temporal association (figures 1 and 2 and online supplemental figure S1). Using a step model case-crossover analysis for each IP,¹⁰ we calculated the period-adjusted OR and its 95% CI of that IP having been undertaken during the 3-month case period before IE admission compared with the preceding 12-month control period (months 4–15), using a mixed-effects logistic regression model with the patient as a random effect and a fixed effect step parameter at 3 months. To account for potential temporal bias of increasing numbers of IPs being performed, we also calculated an adjusted OR for each IP using a mixed-effects logistic regression model adjusted for date of IE admission (see online supplemental appendix methods). Statistical analyses were performed in Stata V.17, using core packages, and all p values were corrected upwards for multiple comparisons using the Benjamini-Hochberg method.¹¹

Secondary analysis

Sensitivity analyses were performed using 4-month and 6-month case periods (online supplemental tables S7 and S8), and an alternative 'hinge-model' case-crossover analysis was performed (see online supplemental appendix), in which instead of fitting a

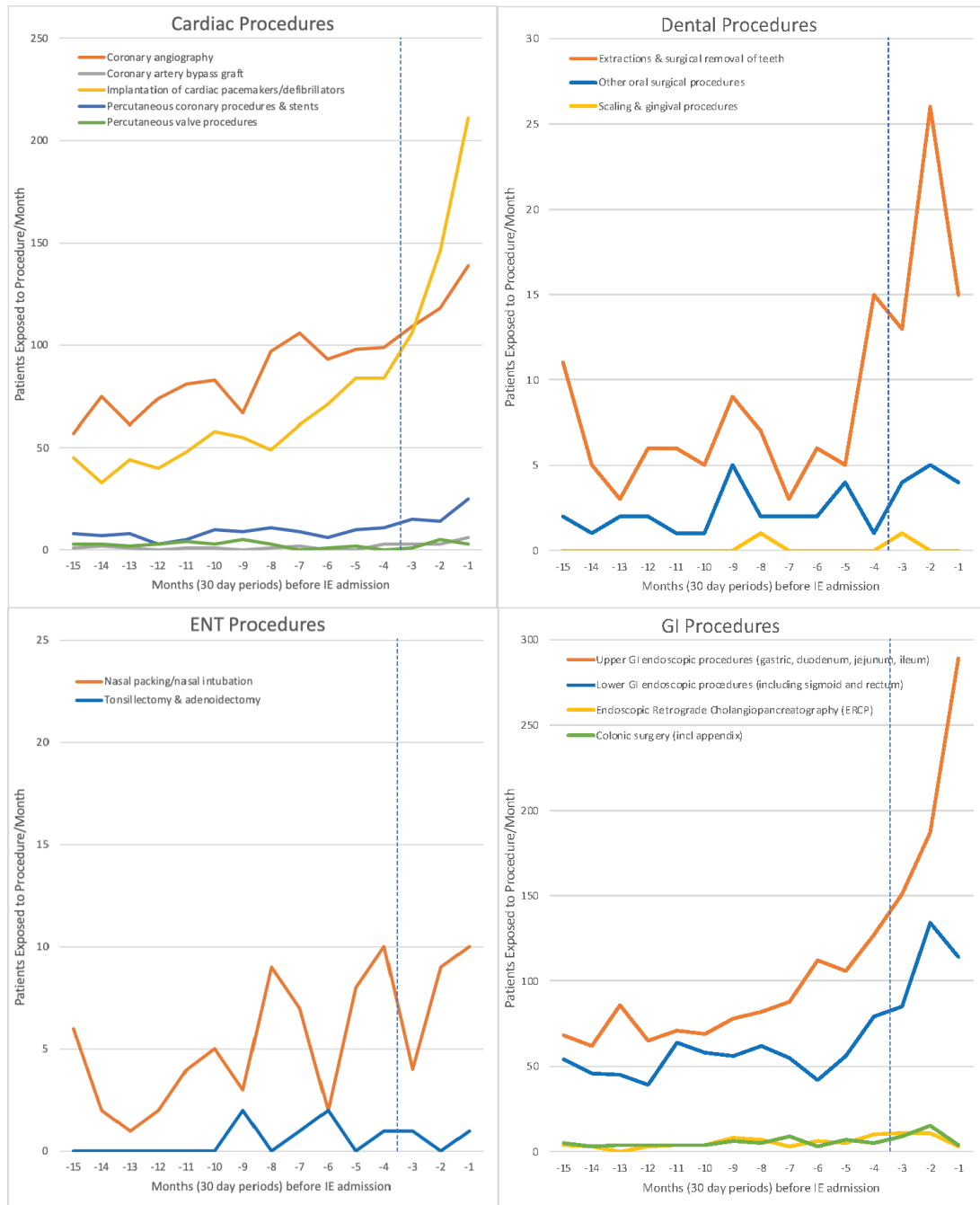


Figure 1 Incidence of different cardiac, dental, ENT and GI invasive procedures over the 15 months before infective endocarditis (IE) hospital admission. Vertical blue dashed line separates case period (months -1 to -3) from control period (months -4 to -15). ENT, ear, nose and throat; GI, gastrointestinal.

step change at 3 months, we fitted a change in the time trend at 3 months before admission (a linear term for months -3 to -1).

Attributable risk

Attributable risk (or absolute risk increase) was defined as the additional number of IE cases per 100 000 procedures) and was estimated for IPs with a significant positive association with IE. The background IE incidence was estimated by dividing the total number of IE cases identified during the study by (duration of study \times 53.4937 million), the latter being the Office of National Statistics figure for the population of England during the middle year of the study (2012). The attributable risk per 100 000 procedures was then calculated as $=100\,000 \times$ background IE

incidence \times (adjusted OR-1)/4, where the adjusted OR from the primary analysis in table 1 and was used to approximate the relative risk for the 3-month case period, and the denominator (4) reflected the case period was one-quarter of a year. The attributable risk was estimated separately for patients at high, moderate or low/unknown risk using previously published prevalence data for these populations (figure 3).^{12 13}

RESULTS

Study population demographics

Between 1 April 2010 and 31 March 2016, there were 14 731 IE admissions (mean age 62.3 years, 66.1% male) in England

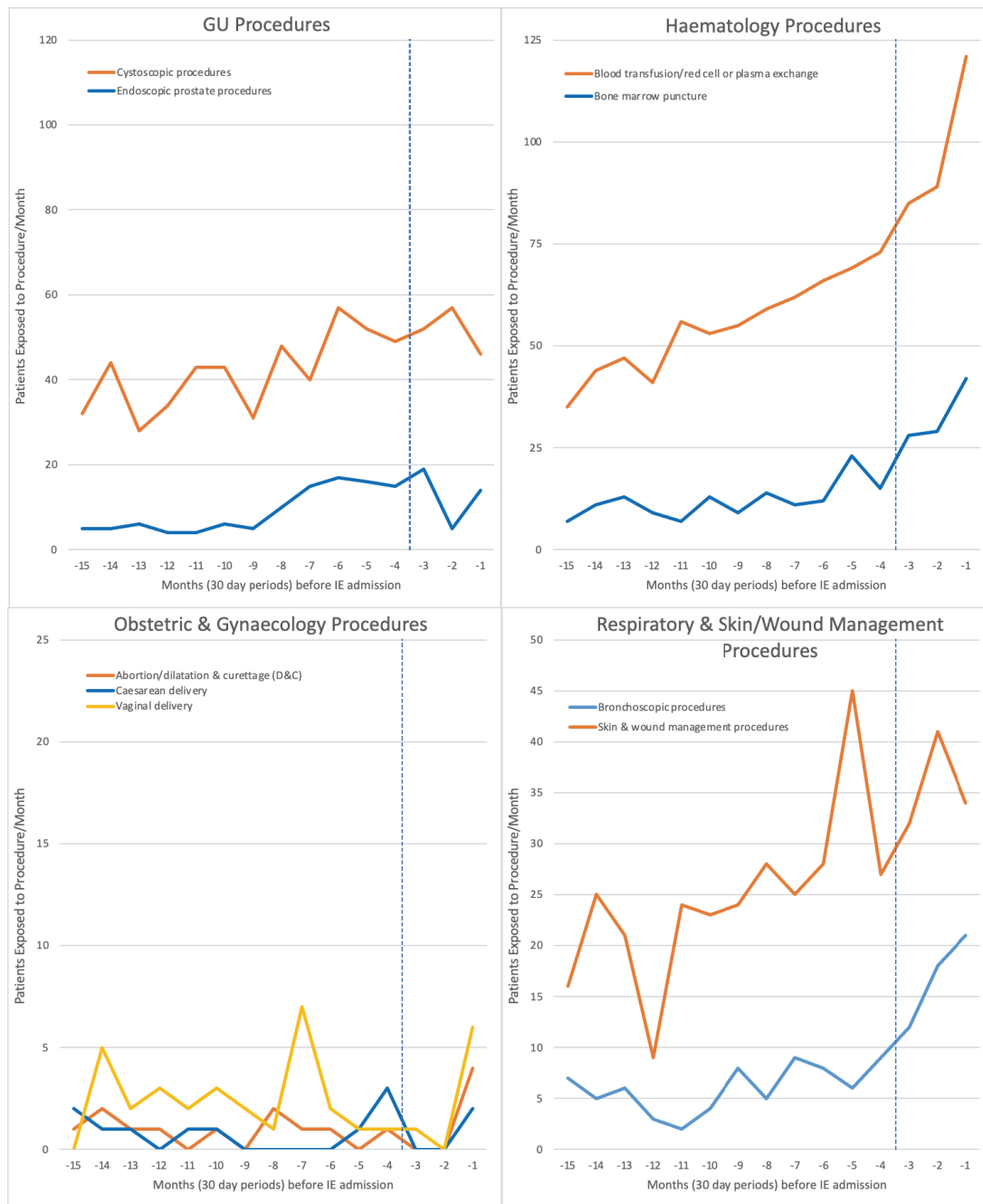


Figure 2 Incidence of different GU, haematology, obstetrics and gynaecology, respiratory and skin/wound management invasive procedures over the 15 months before infective endocarditis (IE) hospital admission. Vertical blue dashed line separates case period (months –1 to –3) from control period (months –4 to –15). GU, genitourinary.

(table 2). Twenty-one per cent occurred in individuals at high IE risk, 17.0% at moderate risk and 61.7% in those at low/unknown risk. Time course studies plotting the monthly incidence of each IP over 15 months before IE admission are shown in figures 1 and 2.

Case-crossover analysis

Case-crossover analysis (table 1) showed that many IPs had no significant IE association. However, our primary step model analysis identified a significant IE association following implantation of cardiac pacemakers/defibrillators (CIEDs) (OR 1.54, 95% CI 1.27 to 1.85, $p < 0.001$), extractions/surgical tooth removal (OR 2.14, 95% CI 1.22 to 3.76, $p = 0.047$), upper GI (OR

1.58, 95% CI 1.34 to 1.85, $p < 0.001$) and lower GI endoscopic procedures (OR 1.66, 95% CI 1.35 to 2.04, $p < 0.001$) and bone marrow biopsy (OR 1.76, 95% CI 1.16 to 2.69, $p = 0.039$). All except extractions/surgical tooth removal were also significantly associated with IE using the alternative hinge model analysis. Hinge model analysis also demonstrated a significant association with IE following blood transfusion/red cell or plasma exchange (OR 1.2, 95% CI 1.07 to 1.35, $p = 0.012$) and bronchoscopic procedures (OR 1.33, 95% CI 1.06 to 1.68, $p = 0.049$). In the sensitivity analyses, extractions and upper and lower gastrointestinal (GI) endoscopy remained significantly associated with IE when a 4-month (but not a 6 month) case period was used (online supplemental tables S6 and S7). The remaining procedures were

Table 1 Case-crossover analysis comparing the incidence of invasive procedures (IPs) in the 3-month case period and the preceding 12-month control period for 14 731 patients admitted with IE

Invasive procedures (ISPs)	Case period (3 m)		Control period (12 m)		Unadjusted step model†		Adjusted step model‡			Adjusted hinge model§		
	Total proc*	Proc/m*	Total proc*	Proc/m*	OR	95% CI	OR	95% CI	P value	OR	95% CI	P value
Cardiac procedures												
Coronary angiography	366	122	991	82.6	1.48	1.31 to 1.67	1.05	0.88 to 1.25	0.776	1.04	0.97 to 1.12	0.403
Coronary artery bypass graft (CABG)	12	4	12	1	4	1.80 to 8.91	2.99	0.75 to 11.96	0.253	1.62	0.96 to 2.73	0.132
Percutaneous coronary procedures and stent implantation	54	18	97	8.1	2.25	1.61 to 3.15	1.59	0.94 to 2.68	0.211	1.28	1.03 to 1.58	0.066
Implantation of cardiac pacemakers/defibrillators	463	154.3	672	56	2.81	2.50 to 3.17	1.54	1.27 to 1.85	<0.001	1.29	1.19 to 1.39	<0.001
Percutaneous valve procedures	9	3	29	2.4	1.25	0.59 to 2.66	2.57	0.78 to 8.45	0.278	1.61	0.99 to 2.60	0.115
Dental procedures												
Extractions or surgical removal of teeth	54	18	81	6.8	2.68	1.90 to 3.78	2.14	1.22 to 3.76	0.047	1.27	1.02 to 1.59	0.082
Other oral surgical procedures	13	4.3	25	2.1	2.10	1.07 to 4.12	1.59	0.56 to 4.53	0.590	1.14	0.75 to 1.75	0.687
Scaling and gingival procedures	1	0.3	1	0.1	4	0.25 to 63.92	2.99	0.02 to 363.52	0.753	0.55	0.08 to 4.04	0.611
ENT procedures												
Tonsillectomy and adenoidectomy	2	0.7	6	0.5	1.33	0.27 to 6.61	0.28	0.03 to 2.39	0.472	0.58	0.21 to 1.56	0.376
Nasal packing/nasal intubation	23	7.7	59	4.9	1.60	0.97 to 2.64	0.71	0.35 to 1.44	0.572	0.99	0.73 to 1.33	0.925
GI procedures												
Upper GI endoscopic procedures (gastric, duodenum, jejunum, ileum)	627	209	1014	84.5	2.59	2.34 to 2.87	1.58	1.34 to 1.85	<0.001	1.30	1.22 to 1.39	<0.001
Lower GI endoscopic procedures (including sigmoid and rectum)	333	111	656	54.7	2.07	1.81 to 2.37	1.66	1.35 to 2.04	<0.001	1.23	1.13 to 1.34	<0.001
Colonic surgery (including appendectomy)	28	9.3	59	4.9	1.9	1.21 to 2.98	1.48	0.74 to 2.95	0.467	1.01	0.76 to 1.35	0.911
Endoscopic retrograde cholangio-pancreatic procedures	25	8.3	57	4.8	1.81	1.12 to 2.94	0.94	0.46 to 1.89	0.853	0.78	0.57 to 1.06	0.198
GU procedures												
Cystoscopy procedures	155	51.7	501	41.8	1.26	1.05 to 1.53	0.92	0.70 to 1.20	0.775	0.94	0.83 to 1.05	0.391
Endoscopic prostate procedures	38	12.7	108	9	1.41	0.97 to 2.05	0.55	0.33 to 0.92	0.084	0.72	0.57 to 0.91	0.019
Haematology procedures												
Blood transfusion/red cell/plasma exchange	295	98.3	660	55	2.84	2.35 to 3.43	1.33	1.01 to 1.76	0.129	1.2	1.07 to 1.35	0.012
Bone marrow puncture	99	33	144	12	2.96	2.27 to 3.87	1.76	1.16 to 2.69	0.039	1.28	1.08 to 1.52	0.018
Obstetric and gynaecological procedures												
Abortion/dilatation and curettage	4	1.3	11	0.9	1.46	0.46 to 4.63	1.69	0.29 to 9.72	0.754	2.07	0.99 to 4.33	0.120
Vaginal delivery	7	2.3	29	2.4	0.97	0.42 to 2.20	0.96	0.31 to 2.98	0.898	1.34	0.83 to 2.15	0.380
Caesarean delivery	2	0.7	10	0.8	0.8	0.18 to 3.65	0.71	0.10 to 5.24	0.805	1.28	0.56 to 2.94	0.639
Respiratory procedures												
Bronchoscopic procedures	51	17	72	6	2.88	2.00 to 4.13	1.87	1.04 to 3.34	0.118	1.33	1.06 to 1.68	0.049
Skin procedures												
Skin and wound management procedures	107	35.7	295	24.6	1.46	1.17 to 1.83	0.92	0.67 to 1.27	0.765	0.96	0.84 to 1.10	0.600

P values in red=significant positive association between the ISP and subsequent IE after Benjamini-Hochberg correction. P values in purple=significant negative association between ISP and subsequent IE after Benjamini-Hochberg correction.
 *A maximum of one procedure of each type per patient was counted each month.
 †Period-adjusted OR of ISPs in case period (3 months prior to IE admission) compared with the 12 month control period (15 to 4 months prior to IE admission) calculated using a mixed-effects logistic regression model with the patient as the random effect.
 ‡OR of ISPs in case period (3 months prior to IE admission) compared with control period (15 to 4 months prior to IE admission) calculated using a mixed-effects logistic regression model adjusted for the month (1–15) and date of IE admission (with the patient as the random effect).
 §OR of ISPs for each month increase in the case period (3 to 1 months prior to IE admission) compared with control period (15 to 4 months prior to IE admission) calculated using a mixed-effects logistic regression model adjusted for month and date of IE admission (with patient as the random effect).
 IE, infective endocarditis; ISPs, invasive procedures; m, month; proc, procedures.

neither statistically nor clinically significant, comprising small effects (OR below 1.05) and/or infrequent procedures (<10 per month in control periods).

For IPs with evidence of an association with IE, the absolute risk increase (attributable risk) was small for low/unknown risk and moderate risk patients, with estimated attributable risk below 1 per 100 000 procedures for those at low/unknown IE risk and below 4 per 100 000 for those at moderate IE risk (figure 3). The absolute risk was greatest for those at high IE

risk, with the absolute risk being highest for those at high IE risk undergoing dental extractions/surgical removal of teeth (49.5 per 100 000 procedures).

DISCUSSION

Previous IE guidelines recommended AP before various IPs (online supplemental table S1). These recommendations have been successively abandoned due to lack of evidence to support

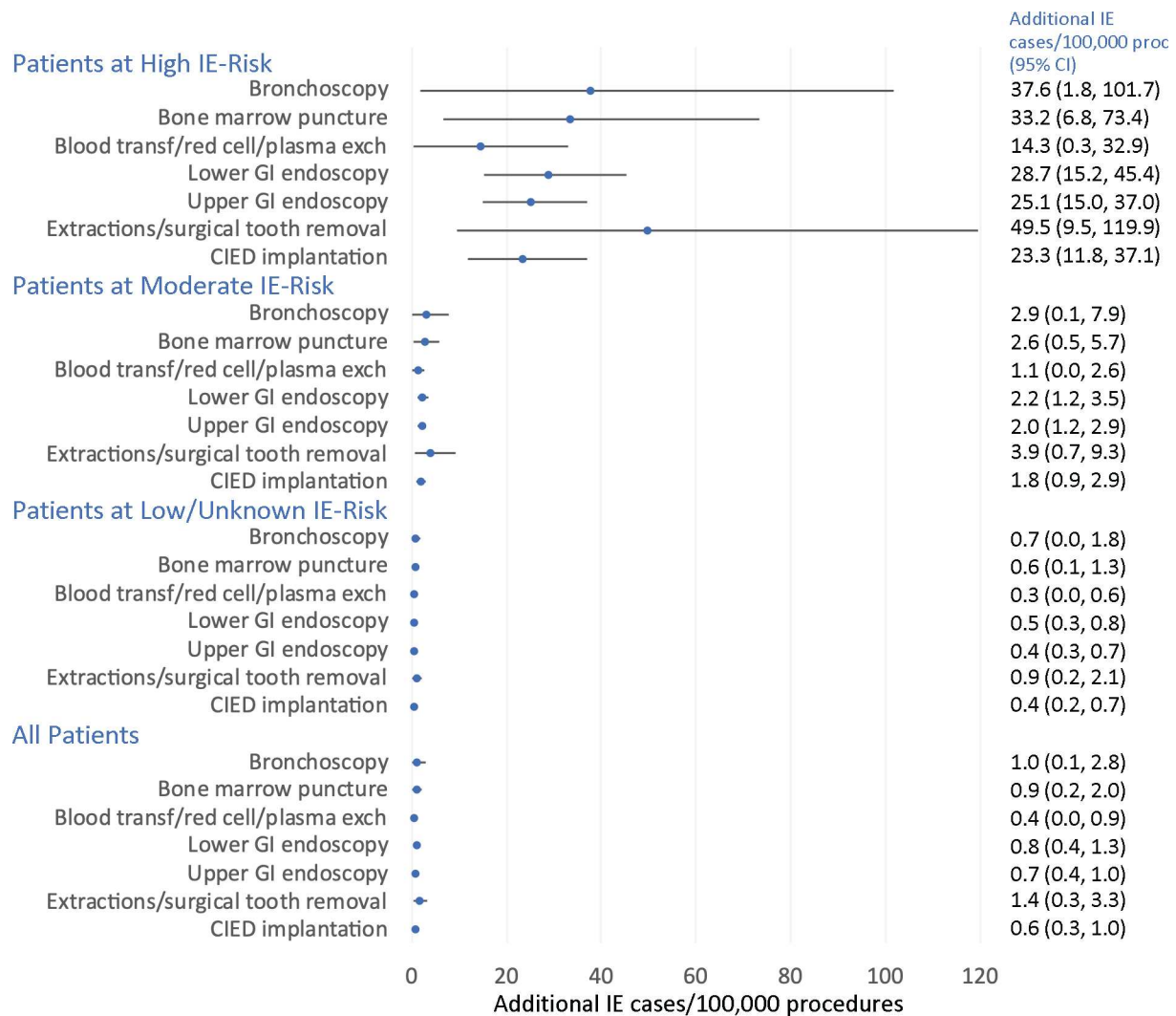


Figure 3 Attributable risk – the predicted additional IE cases per 100 000 procedures by patient risk group. The attributable risk is presented for IPS with a significant positive temporal association with subsequent IE and is expressed as the predicted additional number of IE cases per 100 000 procedures. The population at risk was estimated using the population of England during the middle year of the study (2012–2023) and estimates for the proportion of the population at high, moderate or low/unknown risk. Baseline risk was calculated as the average 3 monthly risk of being subject to each procedure for each population over the study period (March 2010–December 2015, excluding the last 3 months of data). The attributable risk was calculated by multiplying the baseline risk with the adjusted or estimate from table 1. CIED, cardiac implantable electronic devices; exch, exchange; GI, gastrointestinal; IE, infective endocarditis; IPS, invasive procedures; transf, transfusion.

an association between them and subsequent IE. The exception is AP before IDPs in high-risk individuals, which is still recommended outside the UK.^{14 15} A recent Swedish national study, which will be referred to throughout this discussion, found an association between IE and many IPs previously recommended for AP cover, raising the possibility that withdrawal of AP for these may have been premature.⁸ To explore this, we performed a case-crossover study to determine any temporal association between these IPs and subsequent IE.

Cardiac procedures

Device infection is a well-recognised complication of CIED implantation, and surveys suggest that most CIED implantations in England were AP covered.^{16 17} Nonetheless, there was considerable variation in the AP regimens used.^{16 17} Concerns about this led to the first UK CIED infection prevention guidelines in 2015.¹⁸ The incidence of IE following CIED insertion has been calculated at 550 cases/million procedures per year.¹⁹ Despite

it being likely that most CIED implantations were covered by AP, we identified a significantly increased risk of IE in the first 3 months after CIED implantation. The attributable risk was 23.8 per 100 000 procedures for those at high IE risk and 1.8 per 100 000 procedures for those at moderate IE risk. These data suggest that AP cover of CIED implantation was not complete at the time of the study and more may need to be done to improve the effectiveness of CIED infection prevention protocols. It is notable that despite the introduction of UK-wide CIED infection prevention guidelines shortly before the end of this study,¹⁸ current UK IE prevention guidelines contradict these by recommending against the use of AP to prevent IE and failing to mention the IE risk posed by CIED implantation.²⁰

Dental procedures

During the study period, 294 034 IDPs were performed in English hospitals (of which 70.2% were extractions/surgical tooth removal, 23.8% other surgical procedures and 5.6%

Table 2 Clinical characteristics of patients requiring IE admission

Characteristics	Statistics	All IE admissions
Age	N	14722
	Mean (SD)	62.3 (19.9)
	Median (min, max)	67.0 (0, 103)
Sex	N	14731
	Male, n (%)	9734 (66.1)
	Female, n (%)	4997 (33.9)
Level of IE risk before admission	N	14731
	High risk, n (%)	3145 (21.3)
	Moderate risk, n (%)	2503 (17.0)
	Low/unknown risk, n (%)	9083 (61.7)
Reason for high-risk stratification*	Previous IE, n (%)	154 (4.9)
	Previous IE - I38X, n (%)	67 (2.1)
	Replacement heart valve, n (%)	2416 (76.8)
	Repaired heart valve, n (%)	311 (9.9)
	Cyanotic congenital heart disease, n (%)	150 (4.8)
	Repaired congenital heart disease, n (%)	3 (0.1)
	Palliative shunt or conduit, n (%)	37 (1.2)
	Prosthetic heart/ventricular assist device, n (%)	7 (0.2)
	Reason for moderate-risk stratification*	Previous rheumatic fever, n (%)
Non-rheumatic valve disease, n (%)		1571 (62.8)
Congenital valve anomalies, n (%)		58 (2.3)
Hypertrophic cardiomyopathy, n (%)		66 (2.6)
Admission date	N	14731
	Min	01 Apr 2010
	Max	28 Mar 2016
Discharge date	N	14297
	Min	6 April 2010
	Max	31 March 2016
Hospital length of stay (days)*	N	14297
	Mean (SD)	33.0 (27.3)
	Median (min, max)	28 (0, 410)
Discharged alive?	N	14275
	No, n (%)	2677 (18.8)
	Yes, n (%)	11 598 (81.2)

*Length of stay is from admission to discharge alive or until in hospital death. Although we excluded patients discharged alive with a length of stay <3 days, a length of stay <3 days is possible if the patient died within the first 3 days of the IE hospital admission.
IE, infective endocarditis.

scaling procedures). We identified a significant association between extractions/surgical tooth removal and IE. Although no association was identified for other IDPs, the number of these performed in hospital settings was probably too low to detect a significant association. The increase in attributable risk per 100 000 extractions/surgical tooth removal was 49.5 for those at high risk and 3.9 for those at moderate risk. A large recent study of US dentists also demonstrated a significant association between IDPs (particularly extractions and surgical procedures) and IE that was significantly reduced by AP.²¹ Regrettably, a similar study of dentists in England proved impossible due to inadequacies in data recording. Consistent with the previous observations, most guidelines (except NICE) currently recommend AP in high IE risk patients before IDPs.^{9 14 15}

GI procedures

We identified a statistically significant association between upper (gastric, duodenum, jejunum, ileum) and lower (colon, sigmoid,

rectum) GI endoscopic procedures and IE. The increase in attributable risk was, respectively, 25.1 and 28.7 per 100 000 procedures for those at high IE risk undergoing upper or lower GI endoscopy and 2.0 and 2.2 per 100 000 procedures for those at moderate risk. A subanalysis identified no significant difference in the association between upper and lower GI endoscopy and subsequent IE between endoscopic procedures that involved an intervention, for example, a biopsy, and those that did not.

AP was previously recommended before GI endoscopy procedures, and they were also significantly associated with IE in the Swedish study.⁸

Two case series have identified IE following endoscopy,^{22 23} and elevated IE incidence has been noted in elderly high IE risk patients following colonoscopy.²⁴ Nonetheless, current IE prevention guidelines do not recommend AP in these settings. One explanation for an association between colonoscopy and IE is that *Streptococcus gallolyticus* IE is associated with colorectal cancer in the elderly or immunocompromised. Indeed, clinicians are advised to exclude colorectal cancer in patients with *Streptococcus gallolyticus* bacteraemia.²⁵ However, this does not explain the strong association between upper GI endoscopy and IE and could only explain a small proportion of lower GI endoscopy-associated IE.

We found no association between endoscopic retrograde cholangio-pancreatic (ERCP) and IE. This could be because ERCP patients are frequently already receiving antibiotics for cholangitis or because AP to prevent local infection is recommended in several situations for UK patients undergoing ERCP.²⁶

Haematology procedures

There was a significant association in both the primary step and alternative hinge-model analyses between bone marrow biopsy and IE. There was also an association between blood transfusion, red cell or plasma exchange and IE in the hinge analysis. Neither procedure has previously been recommended for AP cover (online supplemental table S1). We included them because the Swedish study found both significantly associated with IE (RR 4.67, 95% CI 1.34 to 16.24, and RR 6.69, 95% CI 4.43 to 10.11, respectively).⁸

Although these associations may be valid, they could also be explained by diagnostic bone marrow biopsy or therapeutic transfusions, particularly if haematological malignancy is suspected in the weeks before an IE diagnosis is confirmed. This is not uncommon since IE may present with features similar to haematological malignancy. Further investigation into this possible association is essential before drawing any conclusions.

Respiratory procedures

Most early guidelines recommended AP before bronchoscopy, and our alternative hinge analysis and the Swedish study⁸ identified an association between bronchoscopy and subsequent IE. Furthermore, our attributable risk estimate was 38 additional IE cases per 100 000 procedures for those at high IE risk. Bacteraemia is a recognised complication of bronchoscopy.²⁷ Nonetheless, consistent with NICE guidance,²⁰ current British Thoracic Society guidelines recommend against the use of AP to prevent IE in those undergoing flexible bronchoscopy.²⁸

Other procedures

We detected no association between ENT, skin or obstetrics and gynaecology procedures and IE. Indeed, the number of these procedures was extremely low over the 15 months before IE admission.

Although cystoscopy and endoscopic prostate procedures were previously recommended for AP cover, and the Swedish study found a significant association between these procedures and IE,⁸ we found no significant association. Antibiotic use to prevent postprocedural urinary tract infections is common and could have masked any relationship in our study. Indeed, another UK study identified a significant association between urological procedures and IE,²⁹ so further investigation is warranted.

Sensitivity analysis

Sensitivity analysis showed the association between extractions, upper or lower GI endoscopy and subsequent IE was sustained for 4 (but not 6) months. The hinge model analysis confirmed the associations identified with the primary step model analysis but identified two more (bronchoscopy and transfusion/red cell/plasma exchange).

The Swedish study did not investigate IDPs, but most IPs we identified as significantly associated with IE were also identified in the Swedish study.⁸ We could not, however, confirm all associations identified in the Swedish study, and the relative risk values they identified were higher than the comparable ORs we found. The reasons for this are: first, the Swedish study screened all inpatient and outpatient IPs to identify associations with IE; we only studied those previously recommended for AP or identified with a positive association in the Swedish study. Second, although both studies used a case-crossover methodology and a 3-month case period, different control periods were used. The Swedish study used a 3-month control period, 1 year before the case period, while we used the preceding 12 months. Sampling the control frequency over an entire year is twice as efficient as sampling equal duration case and control periods.¹⁰ Finally, with increasing numbers of IPs being performed, using a 1-year control period, and adjusting the ORs to take account of the date of each procedure, allowed us to correct for trends in procedure numbers. This means our adjusted ORs are often smaller but may better reflect any actual association between these IP and IE.

Study limitations

Misclassification is possible in administrative databases, particularly for challenging diagnoses such as IE. Nonetheless, a recent analysis of English IE admissions showed that the IE definition we used had the best overall balance between sensitivity, positive predictive value (PPV) and negative predictive value (NPV) for identifying modified Duke criteria positive IE cases (sensitivity 0.65, specificity 0.91, PPV 0.80, NPV 0.82).⁷ Administrative databases also afford larger sample sizes, and this study captured the entire spectrum of IE-related hospitalisations in England, removing the potential for referral bias. Furthermore, case-crossover analysis with constant intrasubject characteristics (eg, age, sex, comorbidities), and each individual serving as their control, eliminated control selection bias and confounding.³⁰

Although our study recorded all IPs performed, this was not the case for IDPs. Most dental procedures are performed in general dental practice and only a minority in hospitals. This may explain our failure to detect an association between some IDPs and IE and could underestimate any association. Nonetheless, we demonstrated a significant association between extractions (including surgical tooth removal) and subsequent IE.

Our study used ICD-10 and OPCS-4 codes to stratify IE cases into those previously at high, moderate or low/unknown IE risk. However, records of predisposing procedures or conditions were incomplete before January 2000, resulting in the potential

misclassification of some high-risk or moderate-risk individuals as low/unknown risk.

Although we wanted to provide details of the causal organisms for IE cases, this proved impossible since there is no requirement to record secondary or supplemental ICD-10 codes on which causal organism data depend and were missing in many cases. This, and the lack of specific ICD-10 codes for oral viridans group streptococci, enterococci and other organisms, made the accurate evaluation of IE microbiology impossible.

CONCLUSIONS

We report a significant association between implantation of CIEDs, upper and lower GI endoscopy, bronchoscopy, and dental extractions (including surgical tooth removal), and subsequent IE. These procedures resulted in an additional 14.3–49.5 IE cases/100 000 procedures in those at high IE risk and an additional 1.1–3.9 IE cases/100 000 procedures in those at moderate risk. These data support a reconsideration of the possible role of preprocedural AP for these procedures in those at high IE risk.

Contributors MHT and JN conceived the idea of the study and formulated the study design. MD, BDP, PL and LB provided the clinical input needed to identify the data to extract. AC, RC and TS undertook data extraction. JN, MB and ECL performed the statistical analysis. JN and MB supervised the analysis. MHT, JN, MD, BDP, PL and LB interpreted the findings. VF provided logistical coordination and support. MT drafted the manuscript. JN, AC, RC, TS, VF, MD, BDP, PL and LB critically reviewed the manuscript, and MT revised the manuscript for final submission. All authors have approved the final draft of the manuscript. MT is the guarantor. MT and JN accept full responsibility for the work and the conduct of the study, had access to the data and controlled the decision to publish. The corresponding author attests that all listed authors meet the authorship criteria and that no others meeting the criteria have been omitted.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by UK National Research Ethics Service. Reference No: 17/SC/0371. Data were obtained from a national database – NHS Digital, and we had both ethics (national research ethics) and Confidentiality Advisory Group permission to use non-identifiable data from the NHS Digital database for this project without the need to seek individual patient consent.

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Data availability statement No data are available. The original data (from which the aggregated data shown in this report are derived) are the subject of data sharing agreements between the University of Sheffield and NHS Digital. These agreements restrict data sharing and require its destruction after study completion. We are therefore unable to share the original data, but they may be obtained by application to NHS Digital (<https://digital.nhs.uk>) after appropriate regulatory approval.

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REFERENCES

- Thornhill MH, Dayer MJ, Nicholl J, et al. An alarming rise in incidence of infective endocarditis in England since 2009: why? *Lancet* 2020;395:1325–7.
- Talha KM, Baddour LM, Thornhill MH, et al. Escalating incidence of infective endocarditis in Europe in the 21st century. *Open Heart* 2021;8:e001846.
- Cahill TJ, Harrison JL, Jewell P, et al. Antibiotic prophylaxis for infective endocarditis: a systematic review and meta-analysis. *Heart* 2017;103:937–44.
- Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American heart association: a guideline from the American heart association rheumatic fever, endocarditis, and Kawasaki disease Committee, Council on cardiovascular disease in the young, and the Council on clinical cardiology, Council on cardiovascular surgery and anesthesia, and the quality of care and outcomes research interdisciplinary working group. *Circulation* 2007;116:1736–54.
- Habib G, Hoen B, Tornos P, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the task force on the prevention, diagnosis, and treatment of infective endocarditis of the European Society of Cardiology (ESC), endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. *Eur Heart J* 2009;30:2369–413.
- National Institute for Health and Care Excellence (NICE). Prophylaxis against infective endocarditis. Clinical Guideline [CG64]. NICE Clinical Guideline No 64 2008.
- Fawcett N, Young B, Peto L, et al. 'Caveat emptor': the cautionary tale of endocarditis and the potential pitfalls of clinical coding data—an electronic health records study. *BMC Med* 2019;17:169.
- Janszky I, Gémes K, Ahnve S, et al. Invasive procedures associated with the development of infective endocarditis. *J Am Coll Cardiol* 2018;71:2744–52.
- National Institute for Health and Care Excellence (NICE). Prophylaxis against infective endocarditis. 2016:NICE Clinical Guideline No 64.
- Mittleman MA, Maclure M, Robins JM. Control sampling strategies for case-crossover studies: an assessment of relative efficiency. *Am J Epidemiol* 1995;142:91–8.
- Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J Royal Statist Soc* 1995;57:289–300.
- Thornhill MH, Gibson TB, Cutler E, et al. Antibiotic prophylaxis and incidence of endocarditis before and after the 2007 AHA recommendations. *J Am Coll Cardiol* 2018;72:2443–54.
- Thornhill MH, Jones S, Prendergast B, et al. Quantifying infective endocarditis risk in patients with predisposing cardiac conditions. *Eur Heart J* 2018;39:586–95.
- Habib G, Lancellotti P, Antunes MJ. ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC) Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J* 2015;2015:3075–128.
- Wilson WR, Gewitz M, Lockhart PB, et al. Prevention of viridans group streptococcal infective endocarditis: a scientific statement from the American Heart Association. *Circulation* 2021;143:e963–78.
- Lowe E, Tayebjee MH, Pratty J, et al. Survey of antibiotic prophylaxis for implantable cardiac electronic device (ICED) insertion in England. *Int J Cardiol* 2012;157:286–7.
- Khan NK, Subramaniam V, Hee C. Antibiotic prophylaxis for permanent pacemaker implantation: an observational study of practice in England. *Br J Cardiol* 2010;17:144–7.
- Sandoe JAT, Barlow G, Chambers JB, et al. Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection. Report of a joint Working Party project on behalf of the British Society for Antimicrobial Chemotherapy (BSAC, host organization), British Heart Rhythm Society (BHRS), British Cardiovascular Society (BCS), British Heart Valve Society (BHVS) and British Society for Echocardiography (BSE). *J Antimicrob Chemother* 2015;70:325–59.
- Duval X, Selson-Suty C, Alla F, et al. Endocarditis in patients with a permanent pacemaker: a 1-year epidemiological survey on infective endocarditis due to valvular and/or pacemaker infection. *Clin Infect Dis* 2004;39:68–74.
- National Institute for Health and Care Excellence (NICE). Prophylaxis against infective endocarditis. NICE Clinical Guideline No 64 2015.
- Thornhill MH, Gibson TB, Yoon F. Infective endocarditis, invasive-dental procedures and antibiotic prophylaxis: case-crossover and cohort studies in a US population. *J Am Coll Cardiol* 2022;80:1029–41 <https://www.ncbi.nlm.nih.gov/pubmed/35987887>
- Breuer GS, Yinnon AM, Halevy J. Infective endocarditis associated with upper endoscopy: case report and review. *J Infect* 1998;36:342–4.
- Karvaj M, Krcmery V, Kisac P. Infective endocarditis after endoscopy. *Scand J Infect Dis* 2010;42:639–40.
- García-Albéniz X, Hsu J, Lipsitch M, et al. Colonoscopy and risk of infective endocarditis in the elderly. *J Am Coll Cardiol* 2016;68:570–1.
- Pasquereau-Kotula E, Martins M, Aymeric L, et al. Significance of *Streptococcus gallolyticus* subsp. *gallolyticus* association with colorectal cancer. *Front Microbiol* 2018;9:614.
- Allison MC, Sandoe JAT, Tighe R, et al. Antibiotic prophylaxis in gastrointestinal endoscopy. *Gut* 2009;58:869–80.
- Yigla M, Oren I, Bentur L, et al. Incidence of bacteraemia following fiberoptic bronchoscopy. *Eur Respir J* 1999;14:789–91.
- Du Rand IA, Blaikley J, Booton R, et al. British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults: accredited by NICE. *Thorax* 2013;68:i1–44.
- Mohee AR, West R, Baig W, et al. A case-control study: are urological procedures risk factors for the development of infective endocarditis? *BJU Int* 2014;114:118–24.
- Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. *Am J Epidemiol* 1991;133:144–53.

Supplementary Appendix

Temporal Association Between Invasive Procedures and Infective Endocarditis

Brief Title – Endocarditis and invasive procedures

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Abbreviations:

AHA = American Heart Association

AP = Antibiotic prophylaxis

BCS = British Cardiac Society

BSAC = British Society for Antimicrobial Chemotherapy

CABG = Coronary artery bypass graft

CI = Confidence interval

ENT = Ear nose and throat

ESC = European Society for Cardiology

ERCP = Endoscopic retrograde cholangio-pancreatic procedures

IDPs = Invasive-dental procedures

IPs = Invasive procedures

IE = Infective endocarditis

NICE = National Institute for Health and Care Excellence

OR = Odds ratio

RR = Relative risk

UK = United Kingdom

US = United States of America

Supplementary Methods

Analyses:

Case-Crossover studies compare exposure to possible trigger events (in this case the incidence of invasive procedures [IP]) for an outcome (in this case admission for infective endocarditis [IE]) during an exposure window (in this case the 3-month case-period before hospital admission for infective endocarditis [IE]) when exposure may lead to the outcome and compares this with the exposure in an earlier control-period (in this case the incidence of IP in the 12 months preceding the case-period). In its simplest form this involves comparing the monthly incidence of the IP in the case-period with the incidence in the control period. If a causal relationship exists between the IP and the outcome IE, then one would expect the mean IP incidence in the case-period to exceed the mean IP incidence in the control-period i.e., there would be a step increase in the IP incidence in the control period on transitioning into the case period. Hence the term “step-model”. This is depicted in the figure below by the graph labelled ‘Sep-Model’. The step increase between the control and case period means can be seen. This is what we describe as the unadjusted “step-model”.

Unadjusted step-model analysis:

For each procedure, the binary outcome (procedure occurred, yes/no) was modelled longitudinally. Whilst it is possible to have multiple procedures within the same month, the vast majority of procedures considered here occur only once if at all. Furthermore, multiple procedures within the same month are likely to relate to one episode for these procedures. For both of these reasons, (simplicity and avoidance of double counting) we chose to limit analysis to yes/no incidence. The unadjusted model considers the probability of an invasive procedure during a month within the “case period” (3 months prior to IE), compared to the probability of an invasive procedure in the remaining months of the study (4-15 prior to IE). This is referred to as a “step-model” as the proportion of patients undergoing a procedure is assumed to follow a step-change once the patient enters the case period:

$$\text{logit}(p_{it}) = \alpha + \beta_{\text{case}} \times I_{(t)} + \gamma_i$$

Where p_{it} denotes the probability that the i^{th} patient recorded a procedure in time-period t (1 to 15), $I_{(t)}$ is equal to 1 if the current timepoint is within 3 months of the IE and 0 otherwise, β_{case} is the coefficient (log-odds) for the procedure in the case period compared to the non-case period, γ_i is a Normally distributed random effect γ_i specific to the patient. This analysis compares monthly occurrence during “case” periods to “control” periods but is biased (exaggerated) if the incidence of procedures increases with time.

To address this, we defined an adjusted ‘step model’ as our primary outcome. This corrected for the background increase in IP incidence and is represented in the figure below by the graph labelled ‘Adjusted Step-Model’. Despite adjusting for the background increase in IP incidence, there is still a step increase in the incidence between the case- and control-periods caused by any association between the IP and subsequent IE (hence the term adjusted “step-model”). The important thing to note is that the unadjusted “step-model” (that represents most case-crossover studies on this subject e.g., the Janszky study (Janszky et al, J. Am. Coll.

Cardiol. (2018) 71(24)2744-2752)) will tend to exaggerate or overestimate the Odds or RR in a situation where the incidence of the potential trigger (IP in this case) is increasing over time. Whereas the adjusted “step-model” (our primary outcome) helps to correct for this but results in a lower OR/RR, – as discussed in the last two sentences of the Discussion section on ‘Sensitivity Analysis’.

Adjusted step-model analysis:

The adjusted model builds on the unadjusted model which also incorporates the association between procedure and calendar time:

$$\text{logit}(p_{it}) = \alpha + \beta_{case} \times I_{(t)} + \beta_{time} \times d_t + \gamma_i$$

Where d_t is the calendar date (1st April 2010 to 31st March 2016), β_{time} is the coefficient (log-odds) for the temporal association, and p_{it} , $I_{(t)}$ and γ_i are as above. This analysis models associations both temporally and with procedure but models the change as a jump at three months prior to IE and was chosen as our primary analysis.

An alternative approach is to consider the slope of the IP incidence in the case- and control-periods as continuous (i.e., without a step change) but with a change of slope (or trajectory) occurring at the point of transition from the control- to the case-period (i.e., with a hinge point in the slope). This is depicted in the figure below by the graph labelled ‘Hinge-model’.

Hinge-model analysis:

The hinge-model analysis allows a gradual separation of the curves during the case period, as opposed to the step (or “jump”) the previous two models. Like the adjusted step-model, this also incorporates the association between procedure and calendar time:

$$\text{logit}(p_{it}) = \alpha + \beta_{case} \times I_{(t)} \times t^* + \beta_{time} \times d_t + \gamma_i$$

Where t^* equal to the study month. This analysis is more biologically plausible and most sensitive to detecting an association where one exists but cannot directly estimate the attributable risk. Since we wanted to estimate this, and since the incidence of many procedures appeared to increase with time, the adjusted step-model analysis was selected as our primary analysis.

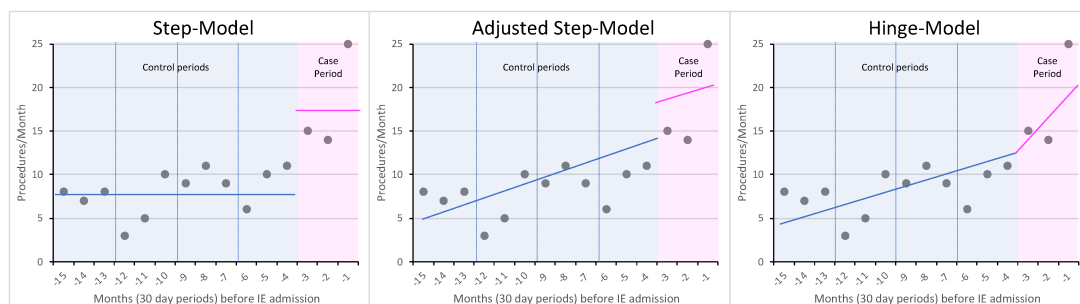


Table S1. Invasive procedures identified for antibiotic prophylaxis by previous guidelines or with positive association with subsequent infective endocarditis

Invasive Procedures (IPs)	BCS 2004[1]	ESC 2004²	AHA 1997³	Janszky et al. 2018⁴ Inpatient IPs RR (95% CI)
GI Procedures				
Upper GI Endoscopy with/without biopsy	✓	-	✓†	3.97 (2.68-5.88)
Lower GI Endoscopy with/without biopsy	✓	-	✓†	2.82 (1.42-5.61)
ERCP (Endoscopic Retrograde Cholangio-Pancreatography)	✓	✓	✓	3.60 (1.34-9.70)
Colonic Surgery	✓	-	✓	-
GU Procedures				
Endoscopic prostate procedures	✓	✓	✓	-
Cystoscopy and endoscopic urological procedures	✓	✓	✓	4.40 (1.67-11.62)
Obstetric & Gynaecological Procedures				
Caesarean section	✓	-	-	-
Vaginal delivery	✓	✓§	✓†	-
Abortion/dilatation and curettage (D&C)	✓	✓§	-	3.00 (1.81-4.98)
Respiratory Procedures				
Bronchoscopic procedures (esp. rigid)	✓	✓	✓	16.00 (2.12-120.65)
Cardiac Procedures				
Implantation of pacemakers/defibrillators	✓	-	-	9.75 (3.48-27.28)
Percutaneous valve procedures	✓	-	-	-
Percutaneous coronary procedures/stents	✓	-	-	3.50 (1.41-8.67)
Coronary artery bypass graft (CABG)	-	-	-	13.8 (5.57-34.21)
Coronary angiography		-	-	4.23 (2.93-6.11)
ENT Procedures				
Tonsillectomy/adenoidectomy	✓	✓	✓	2.33 (0.60-9.02)
Nasal packing/nasal intubation	✓	-	-	-
Dermatological Procedures				
Skin suturing, drainage or wound management	✓	-	-	7.00 (0.86-56.89)
Haematological Procedures				
Blood transfusion/red cell/plasma exchange	-	-	-	6.69 (4.43-10.11)
Bone marrow puncture	-	-	-	4.67 (1.34-16.24)
Dental Procedures				
Dental extractions	✓	✓	✓	-
Other oral surgical procedures	✓	✓	✓	-
Scaling of teeth	✓	✓	✓	-
Endodontic treatment	✓	✓	✓	-

Notes: This table shows those invasive procedures (IPs) for which antibiotic prophylaxis (AP) was recommended for those at moderate- or high-risk of infective endocarditis (IE) (i) by the 2004 British Cardiac Society (BCS) guidance,[1] (ii) by the 2004 European Society for Cardiology (ESC) guidance,[2] or (iii) the 1997 American Heart Association (AHA) guidelines.[3] It also shows the increased relative risk (RR), with 95% Confidence Intervals, of developing IE after different types of IP that was identified in the 2018 analysis of Swedish national data for hospital admissions between January 1998 and December 2011 by Janszky et al.[4] The 2009 ESC guidelines[5] and the 2007 AHA guidelines[6] recommended against the use of AP for all IPs in those at moderate-IE-risk and for all IPs, except dental IPs, in those at high-IE-risk. The 2008 NICE guidelines in the UK recommended the complete cessation of AP for all IPs, including dental procedures.[7] TOE= Transoesophageal echocardiography, ✓ = antibiotic prophylaxis recommended, ✓† = prophylaxis recommended as optional for high-risk patients, ✓§ = antibiotic prophylaxis recommended in the presence of infection.

Table S2.

Codes used to identify those at high-risk of IE. Primary and secondary codes used (except I38X for which primary diagnosis code only was used).

Cardiac Condition	ICD-10 Diagnosis Codes and OPCS-4 Procedure codes For Identifying Those at High-Risk of IE ¹
Previous IE	<p><u>ICD-10 Diagnosis Codes:</u></p> <p>I330 Acute and subacute infective endocarditis I339 Acute endocarditis, unspecified I38X Endocarditis, valve unspecified I390 Endocarditis and mitral valve disorders in disease classified elsewhere I391 Endocarditis and aortic valve disorders in disease classified elsewhere I392 Endocarditis and tricuspid valve disorders in disease classified elsewhere I393 Endocarditis and pulmonary valve disorders in disease classified elsewhere I394 Endocarditis and multiple valve disorders in disease classified elsewhere I398 Endocarditis, valve unspecified in disease classified elsewhere B376 Candidal endocarditis T826 Infection and inflammatory reaction due to cardiac valve prosthesis</p>
Prosthetic replacement of heart valve	<p><u>OPCS-4 Procedure Codes:</u></p> <p>K251 Allograft replacement of mitral valve K252 Xenograft replacement of mitral valve K253 Prosthetic replacement of mitral valve K254 Replacement of mitral valve NEC K261 Allograft replacement of aortic valve K262 Xenograft replacement of aortic valve K263 Prosthetic replacement of aortic valve K264 Replacement of aortic valve NEC K271 Allograft replacement of mitral valve K272 Xenograft replacement of mitral valve K273 Prosthetic replacement of mitral valve K274 Replacement of mitral valve NEC K281 Allograft replacement of pulmonary valve K282 Xenograft replacement of pulmonary valve K283 Prosthetic replacement of pulmonary valve K284 Replacement of pulmonary valve NEC K291 Allograft replacement of valve of heart NEC K292 Xenograft replacement of valve of heart NEC K293 Prosthetic replacement of valve of heart NEC K294 Replacement of valve of heart NEC K297 Replacement of truncal valve K331 Aortic root replacement using pulmonary valve autograft with right ventricle to pulmonary artery valved conduit K332 Aortic root replacement using pulmonary valve autograft with right ventricle to pulmonary artery valved conduit and aortoventriculoplasty K333 Aortic root replacement using homograft K334 Aortic root replacement using mechanical prosthesis K336 Aortoventriculoplasty with pulmonary valve autograft K357 Percutaneous transluminal pulmonary valve replacement</p>
Valve repair using prosthetic material	<p><u>OPCS-4 Procedure Codes:</u></p> <p>K255 Mitral valve repair NEC K258 Other specified plastic repair of mitral valve K259 Unspecified plastic repair of mitral valve K265 Aortic valve repair NEC K268 Other specified plastic repair of aortic valve K269 Unspecified plastic repair of aortic valve K275 Repositioning of tricuspid valve</p>

	<p>K276 Tricuspid valve repair NEC K278 Other specified plastic repair of tricuspid valve K279 Unspecified plastic repair of tricuspid valve K285 Pulmonary valve repair NEC K288 Other specified plastic repair of pulmonary valve K289 Unspecified plastic repair of pulmonary valve K295 Repair of valve of heart NEC K296 Truncal valve repair K298 Other specified plastic repair of unspecified valve of heart K299 Unspecified plastic repair of unspecified valve of heart K301 Revision of plastic repair of mitral valve K302 Revision of plastic repair of aortic valve K303 Revision of plastic repair of tricuspid valve K304 Revision of plastic repair of pulmonary valve K305 Revision of plastic repair of truncal valve K308 Other specified revision of plastic repair of valve of heart K309 Unspecified revision of plastic repair of valve of heart K335 Aortic root replacement NEC K341 Annuloplasty of mitral valve K342 Annuloplasty of tricuspid valve K343 Annuloplasty of valve of heart NEC K358 Other specified therapeutic transluminal operations on valve of heart K359 Unspecified therapeutic transluminal operations on valve of heart</p>
Prosthetic heart or ventricular assist device	<p>OPCS-4 Procedure Codes: K023 Implantation of prosthetic heart K025 Revision of implantation of prosthetic heart K541 Open implantation of ventricular assist device</p>
Congenital Heart Condition (CHC) in whom a palliative shunt or conduit has been used	<p>OPCS-4 Procedure Codes: K041 Repair of tetralogy of Fallot using valved right ventricular outflow conduit K042 Repair of tetralogy of Fallot using right ventricular outflow conduit NEC K063 Left ventricle to aorta tunnel with right ventricle to pulmonary artery valved conduit K171 Total cavopulmonary connection with extracardiac inferior caval vein to pulmonary artery conduit K173 Aortopulmonary reconstruction with systemic to pulmonary arterial shunt K174 Aortopulmonary reconstruction with right ventricle to pulmonary arterial valveless conduit K181 Creation of valved conduit between atrium and ventricle of heart K182 Creation of valved conduit between right atrium and pulmonary artery K183 Creation of valved conduit between right ventricle of heart and pulmonary artery K184 Creation of valved conduit between left ventricle of heart and aorta K185 Revision of valved cardiac conduit K186 Creation of valved conduit between left ventricle of heart pulmonary artery K187 Replacement of valved cardiac conduit K188 Other specified creation of valved cardiac conduit K189 Unspecified creation of valved cardiac conduit K191 Creation of conduit between atrium and ventricle of heart NEC K192 Creation of conduit between right atrium and pulmonary artery NEC K193 Creation of conduit between right ventricle of heart and pulmonary artery NEC K194 Creation of conduit between right ventricle of heart and vena cava K195 Creation of conduit between left ventricle of heart and aorta NEC K196 Revision of cardiac conduit NEC K198 Other specified creation of other cardiac conduit K199 Unspecified creation of other cardiac conduit K761 Percutaneous transluminal balloon dilatation of cardiac conduit K768 Other specified transluminal operations on cardiac conduit K769 Unspecified transluminal operations on cardiac conduit L051 Creation of shunt to main pulmonary artery from ascending aorta using interposition tube prosthesis</p>

	<p>L052 Creation of shunt to right pulmonary artery from ascending aorta using interposition tube prosthesis</p> <p>L053 Creation of shunt to left pulmonary artery from ascending aorta using interposition tube prosthesis</p> <p>L054 Percutaneous transluminal balloon dilatation of interposition tube prosthesis between pulmonary artery and aorta</p> <p>L058 Other specified creation of shunt to pulmonary artery from aorta using interposition tube prosthesis</p> <p>L059 Unspecified creation of shunt to pulmonary artery from aorta using interposition tube prosthesis</p> <p>L071 Creation of shunt to right pulmonary artery from right subclavian artery using interposition tube prosthesis</p> <p>L072 Creation of shunt to left pulmonary artery from left subclavian artery using interposition tube prosthesis</p> <p>L074 Percutaneous transluminal balloon dilatation of interposition tube prosthesis between pulmonary artery and subclavian artery</p> <p>L078 Other specified creation of shunt to pulmonary artery from subclavian artery using interposition tube prosthesis</p> <p>L079 Unspecified creation of shunt to pulmonary artery from subclavian artery using interposition tube prosthesis</p>
Unrepaired cyanotic congenital heart condition (CHC) ²	<p>ICD-10 Diagnosis Codes:</p> <p>Q200 Common arterial trunk</p> <p>Q201 Double outlet right ventricle</p> <p>Q202 Double outlet left ventricle</p> <p>Q203 Discordant ventriculoarterial connection</p> <p>Q204 Double inlet ventricle</p> <p>Q205 Discordant atrioventricular connection</p> <p>Q212 Atrioventricular septal defect</p> <p>Q213 Tetralogy of Fallot</p> <p>Q214 Aortopulmonary septal defect</p> <p>Q262 Total anomalous pulmonary venous connection</p>
Completely repaired CHC defect with prosthetic material or device, whether placed by surgery or catheter intervention, during first 6 months after the procedure only. ³	<p>OPCS-4 Procedure Codes:</p> <p>K091 Repair of defect of atrioventricular septum using dual prosthetic patches</p> <p>K092 Repair of defect of atrioventricular septum using prosthetic patch NEC</p> <p>K101 Repair of defect of interatrial septum using prosthetic patch</p> <p>K111 Repair of defect of interventricular septum using prosthetic patch</p> <p>K117 Repair of defect of inter ventricular septal defect using intraoperative transluminal prosthesis</p> <p>K121 Repair of defect of septum of heart using prosthetic patch NEC</p> <p>K131 Percutaneous transluminal repair of defect of interventricular septum using prosthesis</p> <p>K132 Percutaneous transluminal repair of defect of interventricular septum NEC</p> <p>K133 Percutaneous transluminal repair of defect of interatrial septum using prosthesis</p> <p>K134 Percutaneous transluminal repair of defect of interatrial septum NEC</p> <p>K135 Percutaneous transluminal repair of defect of unspecified septum using prosthesis</p> <p>K138 Other specified transluminal repair of defect of interatrial septum</p> <p>K139 Unspecified transluminal repair of defect of interatrial septum</p> <p>K163 Percutaneous transluminal atrial septum fenestration closure with prosthesis</p> <p>K165 Percutaneous transluminal closure of patent oval foramen with prosthesis</p> <p>L031 Percutaneous transluminal prosthetic occlusion of patent ductus arteriosus</p> <p>L101 Repair of pulmonary artery using prosthesis</p> <p>L233 Plastic repair of aorta using patch graft</p>

Table S3.

Codes used to identify those at moderate-risk of IE

Cardiac Condition	ICD-10 Diagnosis Codes and OPCS-4 Procedure codes For Identifying Those at High-Risk of IE ¹
Previous Rheumatic Fever	<p>ICD-10 Diagnosis Codes:</p> <p>I011 Acute rheumatic endocarditis I018 Other acute rheumatic heart disease I019 Acute rheumatic heart disease, unspecified I020 Rheumatic chorea with heart involvement I050 Rheumatic mitral stenosis I051 Rheumatic mitral insufficiency I052 Rheumatic mitral stenosis with insufficiency I058 Other mitral valve disease I059 Rheumatic mitral valve disease, unspecified I060 Rheumatic aortic stenosis I061 Rheumatic aortic insufficiency I062 Rheumatic aortic stenosis with insufficiency I068 Other rheumatic aortic valve disease I069 Rheumatic aortic valve disease, unspecified I070 Rheumatic tricuspid stenosis I071 Rheumatic tricuspid insufficiency I072 Rheumatic tricuspid stenosis with insufficiency I078 Other rheumatic tricuspid valve disease I079 Rheumatic tricuspid valve disease, unspecified I080 Disorders of both mitral and aortic valves I081 Disorders of both mitral and tricuspid valves I082 Disorders of both aortic and tricuspid valves I083 Combined disorders of mitral, aortic and tricuspid valves I088 Other multiple valve disease I089 Multiple valve diseases, unspecified I090 Rheumatic myocarditis I091 Rheumatic disease of the endocardium, valve unspecified I098 Other specified rheumatic heart disease I099 Rheumatic heart disease, unspecified</p>
Non-Rheumatic Valve Disease	<p>ICD-10 Diagnosis Codes:</p> <p>I340 Mitral valve insufficiency I341 Mitral valve prolapse I342 Nonrheumatic mitral valve stenosis I348 Other nonrheumatic mitral valve disorders I349 Nonrheumatic mitral valve disorder, unspecified I350 Aortic valve stenosis I351 Aortic valve insufficiency I352 Aortic valve stenosis with insufficiency I358 Other nonrheumatic aortic valve disorders I359 Nonrheumatic aortic valve disorder, unspecified I360 Tricuspid valve stenosis I361 Tricuspid valve insufficiency I362 Tricuspid valve stenosis with insufficiency I368 Other nonrheumatic tricuspid valve disorders I369 Nonrheumatic tricuspid valve disorder, unspecified I370 Pulmonary valve stenosis I371 Pulmonary valve insufficiency I372 Pulmonary valve stenosis with insufficiency I378 Other nonrheumatic pulmonary valve disorders I379 Nonrheumatic pulmonary valve disorder, unspecified</p>

Hypertrophic cardiomyopathy	ICD-10 Diagnosis Codes: I421 Obstructive hypertrophic cardiomyopathy I422 Other hypertrophic cardiomyopathy
Congenital valve anomalies	ICD-10 Diagnosis Codes: Q221 Congenital pulmonary valve stenosis Q222 Congenital pulmonary valve insufficiency Q223 Other congenital malformations of pulmonary valve Q224 Congenital tricuspid valve stenosis Q225 Ebstein anomaly Q228 Other congenital malformations of tricuspid valve Q229 Congenital malformations of tricuspid valve, unspecified Q230 Congenital stenosis of aortic valve Q231 Congenital insufficiency of aortic valve Q232 Congenital mitral valve stenosis Q233 Congenital mitral valve insufficiency Q238 Other congenital malformations of aortic and mitral valves Q239 Congenital malformations of aortic and mitral valves, unspecified

Table S4

Summary of Invasive Procedure (IPs) OPCS-4 Codes

Procedures	Paper (RR)*	OPCS-4 Codes	Most Likely Organisms
Haematology Procedures			
Blood transfusion/red cell or plasma exchange	7	X32.1-X34.9 (3 Character – X32–X34)	Staph
Bone marrow puncture	16	W36.5, Y66.7 (Must use 4 character codes)	Staph
GI Procedures			
Oesophageal endoscopic procedures (all)		G14.1-G20.9 U20.2 (3 Character – G14–G20 + U20.2)	
- Transoesophageal echocardiography (TOE)		U20.2	
- Oesophageal endoscopic procedures (excluding TOE)		G14.1-G20.9 (3 Character – G14–G20)	
Upper GI endoscopic procedures (gastric, jejunum, ileum)	4	G42.1-G46.9 G54.1-G55.9 G64.1-G65.9 G79.1-G79.9 G80.1-G80.9 (3 Character – G42-G46, G54-G55, G64-G65 + G79-G80)	Enterococci
Lower GI endoscopic procedures (including sigmoid and rectum)	3	H20.1-28.9 (3 Character – H20–H28)	Enterococci
Colonic surgery (incl appendix)		H01.1-19.9 H29.1-29.9 (3 Character – H01-03 (Appendix), H04–H19 and H29 (Colonic surgery))	
Endoscopic Retrograde Cholangio-pancreatic Procedures (ERCP)		J40-1 - J45.9 (3 Character – J40 - J45)	Enterococci
GU Procedures			
Cystoscopic procedures	4	M09.1-M11.9 M27.1-M30.9 M42.1-M45.9 (3 Character – M09–M11, M27–M30, M42-M45)	Enterococci
Endoscopic prostate procedures		M65.1-M68.9 M70.1-M71.9 (3 Character – M65-M68 and M70-M71)	
Respiratory Procedures			
Bronchoscopic procedures		E48.1-51.9	?

		(3 Character – E48-E51)	
ENT procedures			?
Tonsillectomy & Adenoidectomy	2	E20.1–E20.9 F34.1-34.9, F36.1-F36.9 (3 Character – E20, F34, F36)	?
Nasal packing/nasal intubation		E06.1-E06.9 + X56.1 (3 Character – E06 + 4 char X56.1)	
Obstetric & gynae procedures			?
Abortion/dilatation & curettage (D&C)	3	Q10.1-11.9 (3 Character – Q10, Q11)	
Vaginal delivery		R19.1-24.9 (3 Character – R19-R24)	
Caesarean delivery		R17.1-18.9 (3 Character – R17, R18)	
Cardiac Procedures			
Coronary angiography	4	K63.1-63.9, K65.1-K65.9. (3 Character – K63, K65)	Staph
Coronary artery bypass	14	K40.1-46.9 (3 Character – K40-K46)	Staph
Percutaneous coronary procedures and stents		K49.1-K51.9, K75.1-75.9 (3 Character – K49-51 & K75)	Staph
Implantation of cardiac pacemakers/defibrillators		K59.1-K61.9, K73.1-K73.9 (3 Character – K59-61 & K73)	
Percutaneous valve procedures/heart catheterisation		K35.1-K35.9 (3 Character – K35)	
Skin and wound management procedures	7	S41.1-S42.9, S47.1-S47.9, S54.1-S57.9 (3 Character – S41-42, S47 & S54-57)	Staph
Dental Procedures	N/A		
Extractions & surgical removal of teeth		F09.1-F10.9 (3 Character F09-F10)	OVGS
Other oral surgical procedures		3 Character F01, F02, F03, F04, F05, F06, F08, F11, F18, F22, F23, F24, F26, F28, F29, F30, F32, F38, F39, F40 and 4 Character F42.1-42.3	OVGS
Endodontic procedures		F12.1-F12.9 (3 Character F12)	OVGS
Scaling and gingival procedures		F16.4, F20.1-F20.9 (3 Character F20 + 4 Character F16.4)	OVGS
Restorative Dental Procedures		F13.1-F13.5, F13.8-F13.9 F17.1, F17.6 (Use 4-character codes)	

* Increased relative risk of developing IE within 3 months of this procedure being performed according to the data published by Janszky et al. 2018[4]

Table S5
Individual OPCS-4 Invasive Procedure (IPs) Code Descriptions

Procedure	Code	OPCS-4 Code Description
Cardiac Procedures		
Coronary angiography	K63	Contrast radiology of heart
	K63.1	Angiocardiology of combination of right and left side of heart
	K63.2	Angiocardiology of right side of heart NEC
	K63.3	Angiocardiology of left side of heart NEC
	K63.4	Coronary arteriography using two catheters
	K63.5	Coronary arteriography using single catheter
	K63.6	Coronary arteriography NEC
	K63.8	Other specified contrast radiology of heart
	K63.9	Unspecified contrast radiology of heart
	K65	Catheterisation of heart
	K65.1	Catheterisation of combination of right and left side of heart NEC
	K65.2	Catheterisation of right side of heart NEC
	K65.3	Catheterisation of left side of heart NEC
	K65.4	Catheterisation of left side of heart via atrial transeptal puncture
	K65.8	Other specified catheterisation of heart
	K65.9	Unspecified catheterisation of heart
	Coronary artery bypass	K40
K40.1		Saphenous vein graft replacement of one coronary artery
K40.2		Saphenous vein graft replacement of two coronary arteries
K40.3		Saphenous vein graft replacement of three coronary arteries
K40.4		Saphenous vein graft replacement of four or more coronary arteries
K40.8		Other specified saphenous vein graft replacement of coronary artery
K40.9		Unspecified saphenous vein graft replacement of coronary artery
K41		Other autograft replacement of coronary artery
K41.1		Autograft replacement of one coronary artery NEC
K41.2		Autograft replacement of two coronary arteries NEC
K41.3		Autograft replacement of three coronary arteries NEC
K41.4		Autograft replacement of four or more coronary arteries NEC
K41.8		Other specified other autograft replacement of coronary artery
K41.9		Unspecified other autograft replacement of coronary artery
K42		Allograft replacement of coronary artery
K42.1		Allograft replacement of one coronary artery
K42.2		Allograft replacement of two coronary arteries
K42.3		Allograft replacement of three coronary arteries
K42.4		Allograft replacement of four or more coronary arteries
K42.8		Other specified allograft replacement of coronary artery
K42.9		Unspecified allograft replacement of coronary artery
K43		Prosthetic replacement of coronary artery
K43.1		Prosthetic replacement of one coronary artery
K43.2		Prosthetic replacement of two coronary arteries
K43.3		Prosthetic replacement of three coronary arteries
K43.4		Prosthetic replacement of four or more coronary arteries
K43.8		Other specified prosthetic replacement of coronary artery
K43.9		Unspecified prosthetic replacement of coronary artery
K44		Other replacement of coronary artery
K44.1		Replacement of coronary arteries using multiple methods
K44.2		Revision of replacement of coronary artery
K44.8		Other specified other replacement of coronary artery
K44.9	Unspecified other replacement of coronary artery	
K45	Connection of thoracic artery to coronary artery	
K45.1	Double anastomosis of mammary arteries to coronary arteries	
K45.2	Double anastomosis of thoracic arteries to coronary arteries NEC	

	K45.3	Anastomosis of mammary artery to left anterior descending coronary artery
	K45.4	Anastomosis of mammary artery to coronary artery NEC
	K45.5	Anastomosis of thoracic artery to coronary artery NEC
	K45.6	Revision of connection of thoracic artery to coronary artery
	K45.8	Other specified connection of thoracic artery to coronary artery
	K45.9	Unspecified connection of thoracic artery to coronary artery
	K46	Other bypass of coronary artery
	K46.1	Double implantation of mammary arteries into heart
	K46.2	Double implantation of thoracic arteries into heart NEC
	K46.3	Implantation of mammary artery into heart NEC
	K46.4	Implantation of thoracic artery into heart NEC
	K46.5	Revision of implantation of thoracic artery into heart
	K46.8	Other specified other bypass of coronary artery
	K46.9	Unspecified other bypass of coronary artery
Percutaneous coronary procedures and stents	K49	Transluminal balloon angioplasty of coronary artery
	K49.1	Percutaneous transluminal balloon angioplasty of one coronary artery
	K49.2	Percutaneous transluminal balloon angioplasty of multiple coronary arteries
	K49.3	Percutaneous transluminal balloon angioplasty of bypass graft of coronary artery
	K49.4	Percutaneous transluminal cutting balloon angioplasty of coronary artery
	K49.8	Other specified transluminal balloon angioplasty of coronary artery
	K49.9	Unspecified transluminal balloon angioplasty of coronary artery
	K50	Other therapeutic transluminal operations on coronary artery
	K50.1	Percutaneous transluminal laser coronary angioplasty
	K50.2	Percutaneous transluminal coronary thrombolysis using streptokinase
	K50.3	Percutaneous transluminal injection of therapeutic substance into coronary artery NEC
	K50.4	Percutaneous transluminal atherectomy of coronary artery
	K50.8	Other specified other therapeutic transluminal operations on coronary artery
	K50.9	Unspecified other therapeutic transluminal operations on coronary artery
	K51	Diagnostic transluminal operations on coronary artery
	K51.1	Percutaneous transluminal angioscopy
	K51.2	Intravascular ultrasound of coronary artery
	K51.8	Other specified diagnostic transluminal operations on coronary artery
	K51.9	Unspecified diagnostic transluminal operations on coronary artery
	K75	Percutaneous transluminal balloon angioplasty and insertion of stent into coronary artery
	K75.1	Percutaneous transluminal balloon angioplasty and insertion of 1-2 drug-eluting stents into coronary artery
	K75.2	Percutaneous transluminal balloon angioplasty and insertion of 3 or more drug-eluting stents into coronary artery
	K75.3	Percutaneous transluminal balloon angioplasty and insertion of 1-2 stents into coronary artery
	K75.4	Percutaneous transluminal balloon angioplasty and insertion of 3 or more stents into coronary artery NEC
	K75.8	Other specified percutaneous transluminal balloon angioplasty and insertion of stent into coronary artery
	K75.9	Unspecified percutaneous transluminal balloon angioplasty and insertion of stent into coronary artery
Implantation of cardiac pacemakers/defibrillators	K59	Cardioverter defibrillator introduced through the vein
	K59.1	Implantation of cardioverter defibrillator using one electrode lead
	K59.2	Implantation of cardioverter defibrillator using two electrode leads
	K59.3	Resiting of lead of cardioverter defibrillator
	K59.4	Renewal of cardioverter defibrillator NEC
	K59.5	Removal of cardioverter defibrillator
	K59.6	Implantation of cardioverter defibrillator using three electrode leads
	K59.7	Renewal of cardioverter defibrillator using three electrode leads
	K59.8	Other specified cardioverter defibrillator introduced through the vein
	K59.9	Unspecified cardioverter defibrillator introduced through the vein

	K60	Cardiac pacemaker system introduced through vein
	K60.1	Implantation of intravenous cardiac pacemaker system NEC
	K60.2	Resiting of lead of intravenous cardiac pacemaker system
	K60.3	Renewal of intravenous cardiac pacemaker system NEC
	K60.4	Removal of intravenous cardiac pacemaker system
	K60.5	Implantation of intravenous single chamber cardiac pacemaker system
	K60.6	Implantation of intravenous dual chamber cardiac pacemaker system
	K60.7	Implantation of intravenous biventricular cardiac pacemaker system
	K60.8	Other specified cardiac pacemaker system introduced through vein
	K60.9	Unspecified cardiac pacemaker system introduced through vein
	K61	Other cardiac pacemaker system
	K61.1	Implantation of cardiac pacemaker system NEC
	K61.2	Resiting of lead of cardiac pacemaker system NEC
	K61.3	Renewal of cardiac pacemaker system NEC
	K61.4	Removal of cardiac pacemaker system NEC
	K61.5	Implantation of single chamber cardiac pacemaker system
	K61.6	Implantation of dual chamber cardiac pacemaker system
	K61.7	Implantation of biventricular cardiac pacemaker system
	K61.8	Other specified other cardiac pacemaker system
	K61.9	Unspecified other cardiac pacemaker system
	K73	Other cardiac pacemaker system introduced through vein
	K73.1	Renewal of intravenous single chamber cardiac pacemaker system
	K73.2	Renewal of intravenous dual chamber cardiac pacemaker system
	K73.3	Renewal of intravenous biventricular cardiac pacemaker
	K73.8	Other specified other cardiac pacemaker system introduced through vein
	K73.9	Unspecified other cardiac pacemaker system introduced through vein
Percutaneous valve procedures/heart catheterisation	K35	Therapeutic transluminal operations on valve of heart
	K35.1	Percutaneous transluminal mitral valvotomy
	K35.2	Percutaneous transluminal aortic valvotomy
	K35.3	Percutaneous transluminal tricuspid valvotomy
	K35.4	Percutaneous transluminal pulmonary valvotomy
	K35.5	Percutaneous transluminal valvuloplasty
	K35.6	Percutaneous transluminal pulmonary valve perforation and dilation
	K35.7	Percutaneous transluminal pulmonary valve replacement
	K35.8	Other specified therapeutic transluminal operations on valve of heart
	K35.9	Unspecified therapeutic transluminal operations on valve of heart
GI Procedures		
Trans oesophageal echo (TOE) procedures	U20.2	Transoesophageal echocardiography
Other oesophageal endoscopic procedures	G14	Fibreoptic endoscopic extirpation of lesion of oesophagus
	G14.1	Fibreoptic endoscopic snare resection of lesion of oesophagus
	G14.2	Fibreoptic endoscopic laser destruction of lesion of oesophagus
	G14.3	Fibreoptic endoscopic cauterisation of lesion of oesophagus
	G14.4	Fibreoptic endoscopic injection sclerotherapy to varices of oesophagus
	G14.5	Fibreoptic endoscopic destruction of lesion of oesophagus NEC
	G14.6	Fibreoptic endoscopic submucosal resection of lesion of oesophagus
	G14.7	Fibreoptic endoscopic photodynamic therapy of lesion of oesophagus
	G14.8	Other specified fibreoptic endoscopic extirpation of lesion of oesophagus
	G14.9	Unspecified fibreoptic endoscopic extirpation of lesion of oesophagus
	G15	Other therapeutic fibreoptic endoscopic operations on oesophagus
	G15.1	Fibreoptic endoscopic removal of foreign body from oesophagus
	G15.2	Fibreoptic endoscopic balloon dilation of oesophagus
	G15.3	Fibreoptic endoscopic dilation of oesophagus NEC
	G15.4	Fibreoptic endoscopic insertion of tubal prosthesis into oesophagus
	G15.5	Fibreoptic endoscopic dilation of web of oesophagus
	G15.6	Fibreoptic endoscopic insertion of expanding metal stent into oesophagus NEC
	G15.7	Fibreoptic endoscopic insertion of expanding covered metal stent into oesophagus
	G15.8	Other specified other therapeutic fibreoptic endoscopic operations on oesophagus

	G15.9	Unspecified other therapeutic fibreoptic endoscopic operations on oesophagus
	G16	Diagnostic fibreoptic endoscopic examination of oesophagus
	G16.1	Diagnostic fibreoptic endoscopic examination of oesophagus and biopsy of lesion of oesophagus
	G16.2	Diagnostic fibreoptic endoscopic ultrasound examination of oesophagus
	G16.3	Diagnostic fibreoptic insertion of Bravo pH capsule into oesophagus
	G16.8	Other specified diagnostic fibreoptic endoscopic examination of oesophagus
	G16.9	Unspecified diagnostic fibreoptic endoscopic examination of oesophagus
	G17	Endoscopic extirpation of lesion of oesophagus using rigid oesophagoscope
	G17.1	Endoscopic snare resection of lesion of oesophagus using rigid oesophagoscope
	G17.2	Endoscopic laser destruction of lesion of oesophagus using rigid oesophagoscope
	G17.3	Endoscopic cauterisation of lesion of oesophagus using rigid oesophagoscope
	G17.4	Endoscopic injection sclerotherapy to varices of oesophagus using rigid oesophagoscope
	G17.8	Other specified endoscopic extirpation of lesion of oesophagus using rigid oesophagoscope
	G17.9	Unspecified endoscopic extirpation of lesion of oesophagus using rigid oesophagoscope
	G18	Other therapeutic endoscopic operations on oesophagus using rigid oesophagoscope
	G18.1	Endoscopic removal of foreign body from oesophagus using rigid oesophagoscope
	G18.2	Endoscopic balloon dilation of oesophagus using rigid oesophagoscope
	G18.3	Endoscopic dilation of oesophagus using rigid oesophagoscope NEC
	G18.4	Endoscopic insertion of tubal prosthesis into oesophagus using rigid oesophagoscope
	G18.5	Dilation of web of oesophagus using rigid oesophagoscope
	G18.8	Other specified other therapeutic endoscopic operations on oesophagus using rigid oesophagoscope
	G18.9	Unspecified other therapeutic endoscopic operations on oesophagus using rigid oesophagoscope
	G19	Diagnostic endoscopic examination of oesophagus using rigid oesophagoscope
	G19.1	Diagnostic endoscopic examination of oesophagus and biopsy of lesion of oesophagus using rigid oesophagoscope
	G19.2	Diagnostic endoscopic insertion of Bravo pH capsule using rigid oesophagoscope
	G19.8	Other specified diagnostic endoscopic examination of oesophagus using rigid oesophagoscope
	G19.9	Unspecified diagnostic endoscopic examination of oesophagus using rigid oesophagoscope
	G20	Therapeutic fibreoptic endoscopic operations on oesophagus
	G20.1	Fibreoptic endoscopic coagulation of bleeding lesion of oesophagus
	G20.8	Other specified therapeutic fibreoptic endoscopic operations on oesophagus
	G20.9	Unspecified therapeutic fibreoptic endoscopic operations on oesophagus
Upper GI endoscopic procedures (gastric, jejunum, ileum)	G42*	Other fibreoptic endoscopic extirpation of lesion of upper gastrointestinal tract
	G42.1*	Fibreoptic endoscopic submucosal resection of lesion of upper gastrointestinal tract
	G42.2*	Fibreoptic endoscopic photodynamic therapy of lesion of upper gastrointestinal tract
	G42.3*	Fibreoptic endoscopic mucosal resection of lesion of upper gastrointestinal tract
	G42.8*	Other specified other fibreoptic endoscopic extirpation of lesion of upper gastrointestinal tract
	G42.9*	Unspecified other fibreoptic endoscopic extirpation of lesion of upper gastrointestinal tract
	G43*	Fibreoptic endoscopic extirpation of lesion of upper gastrointestinal tract
	G43.1*	Fibreoptic endoscopic snare resection of lesion of upper gastrointestinal tract
	G43.2*	Fibreoptic endoscopic laser destruction of lesion of upper gastrointestinal tract
	G43.3*	Fibreoptic endoscopic cauterisation of lesion of upper gastrointestinal tract
	G43.4*	Fibreoptic endoscopic sclerotherapy to lesion of upper gastrointestinal tract
	G43.5*	Fibreoptic endoscopic destruction of lesion of upper gastrointestinal tract NEC
	G43.6*	Fibreoptic endoscopic injection therapy to lesion of upper gastrointestinal tract NEC
	G43.7*	Fibreoptic endoscopic rubber band ligation of upper gastrointestinal tract varices

G43.8*	Other specified fibreoptic endoscopic extirpation of lesion of upper gastrointestinal tract
G43.9*	Unspecified fibreoptic endoscopic extirpation of lesion of upper gastrointestinal tract
G44*	Other therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract
G44.1*	Fibreoptic endoscopic insertion of prosthesis into upper gastrointestinal tract
G44.2#	Fibreoptic endoscopic removal of foreign body from upper gastrointestinal tract
G44.3*	Fibreoptic endoscopic dilation of upper gastrointestinal tract NEC
G44.4#	Fibreoptic endoscopic reduction of intussusception of gastroenterostomy
G44.5*	Fibreoptic endoscopic percutaneous insertion of gastrostomy
G44.6*	Fibreoptic endoscopic pressure controlled balloon dilation of lower oesophageal sphincter
G44.7#	Fibreoptic endoscopic removal of gastrostomy tube
G44.8*	Other specified other therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract
G44.9*	Unspecified other therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract
G45#	Diagnostic fibreoptic endoscopic examination of upper gastrointestinal tract
G45.1*	Fibreoptic endoscopic examination of upper gastrointestinal tract and biopsy of lesion of upper gastrointestinal tract
G45.2#	Fibreoptic endoscopic ultrasound examination of upper gastrointestinal tract
G45.3#	Fibreoptic endoscopic insertion of Bravo pH capsule into upper gastrointestinal tract
G45.4#	Fibreoptic endoscopic examination of upper gastrointestinal tract and staining of gastric mucosa
G45.8#	Other specified diagnostic fibreoptic endoscopic examination of upper gastrointestinal tract
G45.9#	Unspecified diagnostic fibreoptic endoscopic examination of upper gastrointestinal tract
G46*	Therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract
G46.1*	Fibreoptic endoscopic endoluminal plication of gastro-oesophageal junction
G46.2*	Fibreoptic endoscopic coagulation of bleeding lesion of upper gastrointestinal tract
G46.8*	Other specified therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract
G46.9*	Unspecified therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract
G54*	Therapeutic endoscopic operations on duodenum
G54.1*	Endoscopic extirpation of lesion of duodenum
G54.2*	Endoscopic dilation of duodenum
G54.3*	Endoscopic insertion of tubal prosthesis into duodenum
G54.8*	Other specified therapeutic endoscopic operations on duodenum
G54.9*	Unspecified therapeutic endoscopic operations on duodenum
G55#	Diagnostic endoscopic examination of duodenum
G55.1*	Diagnostic endoscopic examination of duodenum and biopsy of lesion of duodenum
G55.8#	Other specified diagnostic endoscopic examination of duodenum
G55.9#	Unspecified diagnostic endoscopic examination of duodenum
G64*	Therapeutic endoscopic operations on jejunum
G64.1*	Endoscopic extirpation of lesion of jejunum
G64.2*	Endoscopic dilation of jejunum
G64.3*	Endoscopic insertion of tubal prosthesis into jejunum
G64.8*	Other specified therapeutic endoscopic operations on jejunum
G64.9*	Unspecified therapeutic endoscopic operations on jejunum
G65#	Diagnostic endoscopic examination of jejunum
G65.1*	Diagnostic endoscopic examination of jejunum and biopsy of lesion of jejunum
G65.8#	Other specified diagnostic endoscopic examination of jejunum
G65.9#	Unspecified diagnostic endoscopic examination of jejunum
G79*	Therapeutic endoscopic operations on ileum
G79.1*	Endoscopic extirpation of lesion of ileum
G79.2*	Endoscopic dilation of ileum

	G79.3*	Endoscopic insertion of tubal prosthesis into ileum
	G79.8*	Other specified therapeutic endoscopic operations on ileum
	G79.9*	Unspecified therapeutic endoscopic operations on ileum
	G80 [#]	Diagnostic endoscopic examination of ileum
	G80.1*	Diagnostic endoscopic examination of ileum and biopsy of lesion of ileum
	G80.2 [#]	Wireless capsule endoscopy
	G80.3 [#]	Diagnostic endoscopic balloon examination of ileum
	G80.8 [#]	Other specified diagnostic endoscopic examination of ileum
	G80.9 [#]	Unspecified diagnostic examination of ileum
Lower GI endoscopic procedures (including sigmoid and rectum)	H20*	Endoscopic extirpation of lesion of colon
	H20.1*	Fibreoptic endoscopic snare resection of lesion of colon
	H20.2*	Fibreoptic endoscopic cauterisation of lesion of colon
	H20.3*	Fibreoptic endoscopic laser destruction of lesion of colon
	H20.4*	Fibreoptic endoscopic destruction of lesion of colon NEC
	H20.5*	Fibreoptic endoscopic submucosal resection of lesion of colon
	H20.6*	Fibreoptic endoscopic resection of lesion of colon NEC
	H20.7*	Fibreoptic endoscopic mucosal resection of lesion of colon
	H20.8*	Other specified endoscopic extirpation of lesion of colon
	H20.9*	Unspecified endoscopic extirpation of lesion of colon
	H21*	Other therapeutic endoscopic operations on colon
	H21.1*	Fibreoptic endoscopic dilation of colon
	H21.2*	Fibreoptic endoscopic coagulation of blood vessel of colon
	H21.3 [#]	Fibreoptic endoscopic removal of foreign body from colon
	H21.4*	Fibreoptic endoscopic insertion of expanding metal stent into colon
	H21.5 [#]	Fibreoptic endoscopic decompression of colon
	H21.8*	Other specified other therapeutic endoscopic operations on colon
	H21.9*	Unspecified other therapeutic endoscopic operations on colon
	H22 [#]	Diagnostic endoscopic examination of colon
	H22.1*	Diagnostic fibreoptic endoscopic examination of colon and biopsy of lesion of colon
	H22.8 [#]	Other specified diagnostic endoscopic examination of colon
	H22.9 [#]	Unspecified diagnostic endoscopic examination of colon
	H23*	Endoscopic extirpation of lesion of lower bowel using fibreoptic sigmoidoscope
	H23.1*	Endoscopic snare resection of lesion of lower bowel using fibreoptic sigmoidoscope
	H23.2*	Endoscopic cauterisation of lesion of lower bowel using fibreoptic sigmoidoscope
	H23.3*	Endoscopic laser destruction of lesion of lower bowel using fibreoptic sigmoidoscope
	H23.4*	Endoscopic destruction of lesion of lower bowel using fibreoptic sigmoidoscope NEC
	H23.5*	Endoscopic submucosal resection of lesion of lower bowel using fibreoptic sigmoidoscope
	H23.6*	Endoscopic resection of lesion of lower bowel using fibreoptic sigmoidoscope NEC
	H23.7*	Endoscopic mucosal resection of lesion of lower bowel using fibreoptic sigmoidoscope
	H23.8*	Other specified endoscopic extirpation of lesion of lower bowel using fibreoptic sigmoidoscope
	H23.9*	Unspecified endoscopic extirpation of lesion of lower bowel using fibreoptic sigmoidoscope
	H24*	Other therapeutic endoscopic operations on lower bowel using fibreoptic sigmoidoscope
	H24.1*	Endoscopic dilation of lower bowel using fibreoptic sigmoidoscope
	H24.2*	Endoscopic coagulation of blood vessel of lower bowel using fibreoptic sigmoidoscope
	H24.3*	Endoscopic insertion of tubal prosthesis into lower bowel using fibreoptic sigmoidoscope
	H24.4*	Endoscopic insertion of expanding metal stent into lower bowel using fibreoptic sigmoidoscope
	H24.5 [#]	Endoscopic decompression of lower bowel using fibreoptic sigmoidoscope
	H24.8*	Other specified other therapeutic endoscopic operations on lower bowel using fibreoptic sigmoidoscope

	H24.9*	Unspecified other therapeutic endoscopic operations on lower bowel using fiberoptic sigmoidoscope
	H25 [#]	Diagnostic endoscopic examination of lower bowel using fiberoptic sigmoidoscope
	H25.1*	Diagnostic endoscopic examination of lower bowel and biopsy of lesion of lower bowel using fiberoptic sigmoidoscope
	H25.2 [#]	Diagnostic endoscopic examination of lower bowel and sampling for bacterial overgrowth using fiberoptic sigmoidoscope
	H25.8 [#]	Other specified diagnostic endoscopic examination of lower bowel using fiberoptic sigmoidoscope
	H25.9 [#]	Unspecified diagnostic endoscopic examination of lower bowel using fiberoptic sigmoidoscope
	H26*	Endoscopic extirpation of lesion of sigmoid colon using rigid sigmoidoscope
	H26.1*	Endoscopic snare resection of lesion of sigmoid colon using rigid sigmoidoscope
	H26.2*	Endoscopic cauterisation of lesion of sigmoid colon using rigid sigmoidoscope
	H26.3*	Endoscopic laser destruction of lesion of sigmoid colon using rigid sigmoidoscope
	H26.4*	Endoscopic cryotherapy to lesion of sigmoid colon using rigid sigmoidoscope
	H26.5*	Endoscopic destruction of lesion of sigmoid colon using rigid sigmoidoscope NEC
	H26.6*	Endoscopic submucosal resection of lesion of sigmoid colon using rigid sigmoidoscope
	H26.7*	Endoscopic resection of lesion of sigmoid colon using rigid sigmoidoscope NEC
	H26.8*	Other specified endoscopic extirpation of lesion of sigmoid colon using rigid sigmoidoscope
	H26.9*	Unspecified endoscopic extirpation of lesion of sigmoid colon using rigid sigmoidoscope
	H27*	Other therapeutic endoscopic operations on sigmoid colon using rigid sigmoidoscope
	H27.1*	Endoscopic dilation of sigmoid colon using rigid sigmoidoscope
	H27.2 [#]	Endoscopic removal of foreign body from sigmoid colon using rigid sigmoidoscope
	H27.3 [†]	Endoscopic insertion of tubal prosthesis into sigmoid colon using rigid sigmoidoscope
	H27.4*	Endoscopic insertion of expanding metal stent into sigmoid colon using rigid sigmoidoscope
	H27.5 [#]	Endoscopic decompression of sigmoid colon using rigid sigmoidoscope
	H27.8*	Other specified other therapeutic endoscopic operations on sigmoid colon using rigid sigmoidoscope
	H27.9*	Unspecified other therapeutic endoscopic operations on sigmoid colon using rigid sigmoidoscope
	H28 [#]	Diagnostic endoscopic examination of sigmoid colon using rigid sigmoidoscope
	H28.1*	Diagnostic endoscopic examination of sigmoid colon and biopsy of lesion of sigmoid colon using rigid sigmoidoscope
	H28.8 [#]	Other specified diagnostic endoscopic examination of sigmoid colon using rigid sigmoidoscope
	H28.9 [#]	Unspecified diagnostic endoscopic examination of sigmoid colon using rigid sigmoidoscope
Colonic surgery (incl. appendix)	H01	Emergency excision of appendix
	H01.1	Emergency excision of abnormal appendix and drainage HFQ
	H01.2	Emergency excision of abnormal appendix NEC
	H01.3	Emergency excision of normal appendix
	H01.8	Other specified emergency excision of appendix
	H01.9	Unspecified emergency excision of appendix
	H02	Other excision of appendix
	H02.1	Interval appendectomy
	H02.2	Planned delayed appendectomy NEC
	H02.3	Prophylactic appendectomy NEC
	H02.4	Incidental appendectomy
	H02.8	Other specified other excision of appendix
	H02.9	Unspecified other excision of appendix
	H03	Other operations on appendix

H03.1	Drainage of abscess of appendix
H03.2	Drainage of appendix NEC
H03.3	Exteriorisation of appendix
H03.8	Other specified other operations on appendix
H03.9	Unspecified other operations on appendix
H04	Total excision of colon and rectum
H04.1	Panproctocolectomy and ileostomy
H04.2	Panproctocolectomy and anastomosis of ileum to anus and creation of pouch HFQ
H04.3	Panproctocolectomy and anastomosis of ileum to anus NEC
H04.8	Other specified total excision of colon and rectum
H04.9	Unspecified total excision of colon and rectum
H05	Total excision of colon
H05.1	Total colectomy and anastomosis of ileum to rectum
H05.2	Total colectomy and ileostomy and creation of rectal fistula HFQ
H05.3	Total colectomy and ileostomy NEC
H05.8	Other specified total excision of colon
H05.9	Unspecified total excision of colon
H06	Extended excision of right hemicolon
H06.1	Extended right hemicolectomy and end to end anastomosis
H06.2	Extended right hemicolectomy and anastomosis of ileum to colon
H06.3	Extended right hemicolectomy and anastomosis NEC
H06.4	Extended right hemicolectomy and ileostomy HFQ
H06.5	Extended right hemicolectomy and end to side anastomosis
H06.8	Other specified extended excision of right hemicolon
H06.9	Unspecified extended excision of right hemicolon
H07	Other excision of right hemicolon
H07.1	Right hemicolectomy and end to end anastomosis of ileum to colon
H07.2	Right hemicolectomy and side to side anastomosis of ileum to transverse colon
H07.3	Right hemicolectomy and anastomosis NEC
H07.4	Right hemicolectomy and ileostomy HFQ
H07.5	Right hemicolectomy and end to side anastomosis
H07.8	Other specified other excision of right hemicolon
H07.9	Unspecified other excision of right hemicolon
H08	Excision of transverse colon
H08.1	Transverse colectomy and end to end anastomosis
H08.2	Transverse colectomy and anastomosis of ileum to colon
H08.3	Transverse colectomy and anastomosis NEC
H08.4	Transverse colectomy and ileostomy HFQ
H08.5	Transverse colectomy and exteriorisation of bowel NEC
H08.6	Transverse colectomy and end to side anastomosis
H08.8	Other specified excision of transverse colon
H08.9	Unspecified excision of transverse colon
H09	Excision of left hemicolon
H09.1	Left hemicolectomy and end to end anastomosis of colon to rectum
H09.2	Left hemicolectomy and end to end anastomosis of colon to colon
H09.3	Left hemicolectomy and anastomosis NEC
H09.4	Left hemicolectomy and ileostomy HFQ
H09.5	Left hemicolectomy and exteriorisation of bowel NEC
H09.6	Left hemicolectomy and end to side anastomosis
H09.8	Other specified excision of left hemicolon
H09.9	Unspecified excision of left hemicolon
H10	Excision of sigmoid colon
H10.1	Sigmoid colectomy and end to end anastomosis of ileum to rectum
H10.2	Sigmoid colectomy and anastomosis of colon to rectum
H10.3	Sigmoid colectomy and anastomosis NEC
H10.4	Sigmoid colectomy and ileostomy HFQ
H10.5	Sigmoid colectomy and exteriorisation of bowel NEC
H10.6	Sigmoid colectomy and end to side anastomosis

H10.8	Other specified excision of sigmoid colon
H10.9	Unspecified excision of sigmoid colon
H11	Other excision of colon
H11.1	Colectomy and end to end anastomosis of colon to colon NEC
H11.2	Colectomy and side to side anastomosis of ileum to colon NEC
H11.3	Colectomy and anastomosis NEC
H11.4	Colectomy and ileostomy NEC
H11.5	Colectomy and exteriorisation of bowel NEC
H11.6	Colectomy and end to side anastomosis NEC
H11.8	Other specified other excision of colon
H11.9	Unspecified other excision of colon
H12	Extirpation of lesion of colon
H12.1	Excision of diverticulum of colon
H12.2	Excision of lesion of colon NEC
H12.3	Destruction of lesion of colon NEC
H12.8	Other specified extirpation of lesion of colon
H12.9	Unspecified extirpation of lesion of colon
H13	Bypass of colon
H13.1	Bypass of colon by anastomosis of ileum to colon
H13.2	Bypass of colon by anastomosis of caecum to sigmoid colon
H13.3	Bypass of colon by anastomosis of transverse colon to sigmoid colon
H13.4	Bypass of colon by anastomosis of transverse colon to rectum
H13.5	Bypass of colon by anastomosis of colon to rectum NEC
H13.8	Other specified bypass of colon
H13.9	Unspecified bypass of colon
H14	Exteriorisation of caecum
H14.1	Tube caecostomy
H14.2	Refashioning of caecostomy
H14.3	Closure of caecostomy
H14.4	Appendicocaecostomy
H14.8	Other specified exteriorisation of caecum
H14.9	Unspecified exteriorisation of caecum
H15	Other exteriorisation of colon
H15.1	Loop colostomy
H15.2	End colostomy
H15.3	Refashioning of colostomy
H15.4	Closure of colostomy
H15.5	Dilation of colostomy
H15.6	Reduction of prolapse of colostomy
H15.7	Percutaneous endoscopic sigmoid colostomy
H15.8	Other specified other exteriorisation of colon
H15.9	Unspecified other exteriorisation of colon
H16	Incision of colon
H16.1	Drainage of colon
H16.2	Caecotomy
H16.3	Colotomy
H16.8	Other specified incision of colon
H16.9	Unspecified incision of colon
H17	Intra-abdominal manipulation of colon
H17.1	Open reduction of intussusception of colon
H17.2	Open reduction of volvulus of caecum
H17.3	Open reduction of volvulus of sigmoid colon
H17.4	Open reduction of volvulus of colon NEC
H17.5	Open relief of strangulation of colon
H17.6	Open relief of obstruction of colon NEC
H17.8	Other specified intra-abdominal manipulation of colon
H17.9	Unspecified intra-abdominal manipulation of colon
H18	Open endoscopic operations on colon

	H18.1	Open colonoscopy	
	H18.8	Other specified open endoscopic operations on colon	
	H18.9	Unspecified open endoscopic operations on colon	
	H19	Other open operations on colon	
	H19.1	Open biopsy of lesion of colon	
	H19.2	Fixation of colon	
	H19.3	Enterorrhaphy of colon	
	H19.4	Open removal of foreign body from colon	
	H19.8	Other specified other open operations on colon	
	H19.9	Unspecified other open operations on colon	
	H29	Subtotal excision of colon	
	H29.1	Subtotal excision of colon and rectum and creation of colonic pouch and anastomosis of colon to anus	
	H29.2	Subtotal excision of colon and rectum and creation of colonic pouch NEC	
	H29.3	Subtotal excision of colon and creation of colonic pouch and anastomosis of colon to rectum	
	H29.4	Subtotal excision of colon and creation of colonic pouch NEC	
	H29.5	Subtotal excision of colon and anastomosis of colon to ileum	
	H29.8	Other specified subtotal excision of colon	
	H29.9	Unspecified subtotal excision of colon	
	Endoscopic Retrograde Cholangio-pancreatic Procedures (ERCP)	J40	Endoscopic retrograde placement of prosthesis in bile duct
		J40.1	Endoscopic retrograde insertion of tubal prosthesis into both hepatic ducts
J40.2		Endoscopic retrograde insertion of tubal prosthesis into bile duct NEC	
J40.3		Endoscopic retrograde renewal of tubal prosthesis in bile duct NEC	
J40.4		Endoscopic retrograde removal of tubal prosthesis from bile duct	
J40.5		Endoscopic retrograde insertion of expanding covered metal stent into bile duct	
J40.6		Endoscopic retrograde insertion of expanding metal stent into bile duct NEC	
J40.7		Endoscopic retrograde renewal of expanding metal stent in bile duct	
J40.8		Other specified endoscopic retrograde placement of prosthesis in bile duct	
J40.9		Unspecified endoscopic retrograde placement of prosthesis in bile duct	
J41		Other therapeutic endoscopic retrograde operations on bile duct	
J41.1		Endoscopic retrograde extraction of calculus from bile duct	
J41.2		Endoscopic dilation of bile duct NEC	
J41.3		Endoscopic retrograde lithotripsy of calculus of bile duct	
J41.4		Endoscopic retrograde photodynamic laser therapy of lesion of bile duct	
J41.8		Other specified other therapeutic endoscopic retrograde operations on bile duct	
J41.9		Unspecified other therapeutic endoscopic retrograde operations on bile duct	
J42		Therapeutic endoscopic retrograde operations on pancreatic duct	
J42.1		Endoscopic retrograde insertion of tubal prosthesis into pancreatic duct	
J42.2		Endoscopic retrograde renewal of tubal prosthesis in pancreatic duct	
J42.3		Endoscopic retrograde removal of calculus from pancreatic duct	
J42.4		Endoscopic retrograde drainage of lesion of pancreas	
J42.5		Endoscopic retrograde dilation of pancreatic duct	
J42.8		Other specified therapeutic endoscopic retrograde operations on pancreatic duct	
J42.9		Unspecified therapeutic endoscopic retrograde operations on pancreatic duct	
J43		Diagnostic endoscopic retrograde examination of bile duct and pancreatic duct	
J43.1		Endoscopic retrograde cholangiopancreatography and biopsy of lesion of ampulla of Vater	
J43.2		Endoscopic retrograde cholangiopancreatography and biopsy of lesion of biliary or pancreatic system NEC	
J43.3		Endoscopic retrograde cholangiopancreatography and collection of bile	
J43.8		Other specified diagnostic endoscopic retrograde examination of bile duct and pancreatic duct	
J43.9		Unspecified diagnostic endoscopic retrograde examination of bile duct and pancreatic duct	
J44		Diagnostic endoscopic retrograde examination of bile duct	
J44.1	Endoscopic retrograde cholangiography and biopsy of lesion of bile duct		
J44.8	Other specified diagnostic endoscopic retrograde examination of bile duct		

	J44.9	Unspecified diagnostic endoscopic retrograde examination of bile duct
	J45	Diagnostic endoscopic retrograde examination of pancreatic duct
	J45.1	Endoscopic retrograde pancreatography and biopsy of lesion of pancreas
	J45.2	Endoscopic retrograde pancreatography and collection of pancreatic juice
	J45.3	Endoscopic retrograde pancreatography through accessory ampulla of Vater
	J45.8	Other specified diagnostic endoscopic retrograde examination of pancreatic duct
	J45.9	Unspecified diagnostic endoscopic retrograde examination of pancreatic duct
GU Procedures		
Cystoscopic procedures	M09	Therapeutic endoscopic operations on calculus of kidney
	M09.1	Endoscopic ultrasound fragmentation of calculus of kidney
	M09.2	Endoscopic electrohydraulic shockwave fragmentation of calculus of kidney
	M09.3	Endoscopic laser fragmentation of calculus of kidney
	M09.4	Endoscopic extraction of calculus of kidney NEC
	M09.8	Other specified therapeutic endoscopic operations on calculus of kidney
	M09.9	Unspecified therapeutic endoscopic operations on calculus of kidney
	M10	Other therapeutic endoscopic operations on kidney
	M10.1	Endoscopic extirpation of lesion of kidney NEC
	M10.2	Endoscopic pyeloplasty
	M10.3	Endoscopic deroofing of multiple cysts of kidney
	M10.4	Endoscopic cryoablation of lesion of kidney
	M10.5	Endoscopic endoluminal balloon rupture of stenosis of pelviureteric junction of kidney
	M10.8	Other specified other therapeutic endoscopic operations on kidney
	M10.9	Unspecified other therapeutic endoscopic operations on kidney
	M11	Diagnostic endoscopic examination of kidney
	M11.1	Diagnostic endoscopic examination of kidney and biopsy of lesion of kidney NEC
	M11.2	Diagnostic endoscopic retrograde examination of kidney and biopsy of lesion of kidney
	M11.3	Diagnostic endoscopic retrograde examination of kidney NEC
	M11.8	Other specified diagnostic endoscopic examination of kidney
	M11.9	Unspecified diagnostic endoscopic examination of kidney
	M27	Therapeutic ureteroscopic operations on ureter
	M27.1	Ureteroscopic laser fragmentation of calculus of ureter
	M27.2	Ureteroscopic fragmentation of calculus of ureter NEC
	M27.3	Ureteroscopic extraction of calculus of ureter
	M27.4	Ureteroscopic insertion of ureteric stent
	M27.5	Ureteroscopic removal of ureteric stent
	M27.6	Ureteroscopic endoluminal balloon rupture of stenosis of ureter
	M27.7	Ureteroscopic dilation of ureter
	M27.8	Other specified therapeutic ureteroscopic operations on ureter
	M27.9	Unspecified therapeutic ureteroscopic operations on ureter
	M28	Other endoscopic removal of calculus from ureter
	M28.1	Code retired - refer to introduction
	M28.2	Code retired - refer to introduction
	M28.3	Code retired - refer to introduction
	M28.4	Endoscopic catheter drainage of calculus of ureter
	M28.5	Endoscopic drainage of calculus of ureter by dilation of ureter
	M28.8	Other specified other endoscopic removal of calculus from ureter
	M28.9	Unspecified other endoscopic removal of calculus from ureter
	M29	Other therapeutic endoscopic operations on ureter
	M29.1	Endoscopic extirpation of lesion of ureter
	M29.2	Endoscopic insertion of tubal prosthesis into ureter NEC
	M29.3	Endoscopic removal of tubal prosthesis from ureter
	M29.4	Endoscopic dilation of ureter
	M29.5	Endoscopic renewal of tubal prosthesis into ureter
	M29.8	Other specified other therapeutic endoscopic operations on ureter
	M29.9	Unspecified other therapeutic endoscopic operations on ureter

	M30	Diagnostic endoscopic examination of ureter
	M30.1	Endoscopic retrograde pyelography
	M30.2	Endoscopic catheterisation of ureter
	M30.3	Endoscopic ureteric urine sampling
	M30.4	Nephroscopic ureteroscopy
	M30.5	Diagnostic endoscopic examination of ureter and biopsy of lesion of ureter NEC
	M30.6	Diagnostic endoscopic examination of ureter and biopsy of lesion of ureter using rigid ureteroscope
	M30.8	Other specified diagnostic endoscopic examination of ureter
	M30.9	Unspecified diagnostic endoscopic examination of ureter
	M42	Endoscopic extirpation of lesion of bladder
	M42.1	Endoscopic resection of lesion of bladder
	M42.2	Endoscopic cauterisation of lesion of bladder
	M42.3	Endoscopic destruction of lesion of bladder NEC
	M42.8	Other specified endoscopic extirpation of lesion of bladder
	M42.9	Unspecified endoscopic extirpation of lesion of bladder
	M43	Endoscopic operations to increase capacity of bladder
	M43.1	Endoscopic transection of bladder
	M43.2	Endoscopic hydrostatic distension of bladder
	M43.3	Endoscopic overdistension of bladder NEC
	M43.4	Endoscopic injection of neurolytic substance into nerve of bladder
	M43.8	Other specified endoscopic operations to increase capacity of bladder
	M43.9	Unspecified endoscopic operations to increase capacity of bladder
	M44	Other therapeutic endoscopic operations on bladder
	M44.1	Endoscopic lithopaxy
	M44.2	Endoscopic extraction of calculus of bladder NEC
	M44.3	Endoscopic removal of foreign body from bladder
	M44.4	Endoscopic removal of blood clot from bladder
	M44.8	Other specified other therapeutic endoscopic operations on bladder
	M44.9	Unspecified other therapeutic endoscopic operations on bladder
	M45	Diagnostic endoscopic examination of bladder
	M45.1	Diagnostic endoscopic examination of bladder and biopsy of lesion of bladder NEC
	M45.2	Diagnostic endoscopic examination of bladder and biopsy of lesion of prostate NEC
	M45.3	Diagnostic endoscopic examination of bladder and biopsy of lesion of bladder using rigid cystoscope
	M45.4	Diagnostic endoscopic examination of bladder and biopsy of lesion of prostate using rigid cystoscope
	M45.5	Diagnostic endoscopic examination of bladder using rigid cystoscope
	M45.8	Other specified diagnostic endoscopic examination of bladder
	M45.9	Unspecified diagnostic endoscopic examination of bladder
Endoscopic prostate procedures	M65	Endoscopic resection of outlet of male bladder
	M65.1	Endoscopic resection of prostate using electrotome
	M65.2	Endoscopic resection of prostate using punch
	M65.3	Endoscopic resection of prostate NEC
	M65.4	Endoscopic resection of prostate using laser
	M65.5	Endoscopic resection of prostate using vapotrode
	M65.6	Endoscopic ablation of prostate using steam
	M65.8	Other specified endoscopic resection of outlet of male bladder
	M65.9	Unspecified endoscopic resection of outlet of male bladder
	M66	Other therapeutic endoscopic operations on outlet of male bladder
	M66.1	Endoscopic sphincterotomy of external sphincter of male bladder
	M66.2	Endoscopic incision of outlet of male bladder NEC
	M66.3	Endoscopic injection of inert substance into outlet of male bladder
	M66.8	Other specified other therapeutic endoscopic operations on outlet of male bladder
	M66.9	Unspecified other therapeutic endoscopic operations on outlet of male bladder
	M67	Other therapeutic endoscopic operations on prostate
	M67.1	Endoscopic cryotherapy to lesion of prostate
	M67.2	Endoscopic destruction of lesion of prostate NEC

	M67.3	Endoscopic drainage of prostate
	M67.4	Endoscopic removal of calculus from prostate
	M67.5	Endoscopic microwave destruction of lesion of prostate
	M67.6	Endoscopic radiofrequency ablation of lesion of prostate
	M67.8	Other specified other therapeutic endoscopic operations on prostate
	M67.9	Unspecified other therapeutic endoscopic operations on prostate
	M68	Endoscopic insertion of prosthesis into prostate
	M68.1	Endoscopic insertion of prostatic stent
	M68.2	Endoscopic removal of prostatic stent
	M68.3	Endoscopic insertion of prosthesis to compress lobe of prostate
	M68.8	Other specified endoscopic insertion of prosthesis into prostate
	M68.9	Unspecified endoscopic insertion of prosthesis into prostate
	M70.1	Aspiration of prostate NEC
	M70.2	Perineal needle biopsy of prostate
	M70.3	Rectal needle biopsy of prostate
	M70.4	Balloon dilation of prostate
	M70.5	Massage of prostate
	M70.6	Radioactive seed implantation into prostate
	M70.7	Transurethral radiofrequency needle ablation of prostate
	M70.8	Other specified other operations on outlet of male bladder
	M70.9	Unspecified other operations on outlet of male bladder
	M71	Other operations on prostate
	M71.1	High intensity focused ultrasound of prostate
	M71.2	Implantation of radioactive substance into prostate
	M71.8	Other specified other operations on prostate
	M71.9	Unspecified other operations on prostate
Respiratory Procedures		
Bronchoscopic procedures	E48	Therapeutic fiberoptic endoscopic operations on lower respiratory tract
	E48.1	Fiberoptic endoscopic snare resection of lesion of lower respiratory tract
	E48.2	Fiberoptic endoscopic laser destruction of lesion of lower respiratory tract
	E48.3	Fiberoptic endoscopic destruction of lesion of lower respiratory tract NEC
	E48.4	Fiberoptic endoscopic aspiration of lower respiratory tract
	E48.5	Fiberoptic endoscopic removal of foreign body from lower respiratory tract
	E48.6	Fiberoptic endoscopic irrigation of lower respiratory tract
	E48.7	Fiberoptic endoscopic photodynamic therapy of lesion of lower respiratory tract
	E48.8	Other specified therapeutic fiberoptic endoscopic operations on lower respiratory tract
	E48.9	Unspecified therapeutic fiberoptic endoscopic operations on lower respiratory tract
	E49	Diagnostic fiberoptic endoscopic examination of lower respiratory tract
	E49.1	Diagnostic fiberoptic endoscopic examination of lower respiratory tract and biopsy of lesion of lower respiratory tract
	E49.2	Diagnostic fiberoptic endoscopic examination of lower respiratory tract and lavage of lesion of lower respiratory tract
	E49.3	Diagnostic fiberoptic endoscopic examination of lower respiratory tract and brush cytology of lesion of lower respiratory tract
	E49.4	Diagnostic fiberoptic endoscopic examination of lower respiratory tract with lavage and brush cytology of lesion of lower respiratory tract
	E49.5	Diagnostic fiberoptic endoscopic examination of lower respiratory tract with biopsy, lavage and brush cytology of lesion of lower respiratory tract
	E49.8	Other specified diagnostic fiberoptic endoscopic examination of lower respiratory tract
	E49.9	Unspecified diagnostic fiberoptic endoscopic examination of lower respiratory tract
	E50	Therapeutic endoscopic operations on lower respiratory tract using rigid bronchoscope
	E50.1	Endoscopic snare resection of lesion of lower respiratory tract using rigid bronchoscope
	E50.2	Endoscopic laser destruction of lesion of lower respiratory tract using rigid bronchoscope

	E50.3	Endoscopic destruction of lesion of lower respiratory tract using rigid bronchoscope NEC
	E50.4	Endoscopic aspiration of lower respiratory tract using rigid bronchoscope
	E50.5	Endoscopic removal of foreign body from lower respiratory tract using rigid bronchoscope
	E50.6	Endoscopic irrigation of lower respiratory tract using rigid bronchoscope
	E50.8	Other specified therapeutic endoscopic operations on lower respiratory tract using rigid bronchoscope
	E50.9	Unspecified therapeutic endoscopic operations on lower respiratory tract using rigid bronchoscope
	E51	Diagnostic endoscopic examination of lower respiratory tract using rigid bronchoscope
	E51.1	Diagnostic endoscopic examination of lower respiratory tract and biopsy of lesion of lower respiratory tract using rigid bronchoscope
	E51.8	Other specified diagnostic endoscopic examination of lower respiratory tract using rigid bronchoscope
	E51.9	Unspecified diagnostic endoscopic examination of lower respiratory tract using rigid bronchoscope
ENT procedures		
Tonsillectomy & Adenoidectomy	E20	Operations on adenoid
	E20.1	Total adenoidectomy
	E20.2	Biopsy of adenoid
	E20.3	Surgical arrest of postoperative bleeding of adenoid
	E20.4	Suction diathermy adenoidectomy
	E20.8	Other specified operations on adenoid
	E20.9	Unspecified operations on adenoid
	F34	Excision of tonsil
	F34.1	Bilateral dissection tonsillectomy
	F34.2	Bilateral guillotine tonsillectomy
	F34.3	Bilateral laser tonsillectomy
	F34.4	Bilateral excision of tonsil NEC
	F34.5	Excision of remnant of tonsil
	F34.6	Excision of lingual tonsil
	F34.7	Bilateral coblation tonsillectomy
	F34.8	Other specified excision of tonsil
	F34.9	Unspecified excision of tonsil
	F36	Other operations on tonsil
	F36.1	Destruction of tonsil
	F36.2	Biopsy of lesion of tonsil
	F36.3	Drainage of abscess of peritonsillar region
	F36.4	Removal of foreign body from tonsil
	F36.5	Surgical arrest of postoperative bleeding from tonsillar bed
F36.6	Excision of lesion of tonsil	
F36.8	Other specified other operations on tonsil	
F36.9	Unspecified other operations on tonsil	
Nasal packing/nasal intubation	E06	Packing of cavity of nose
	E06.1	Packing of posterior cavity of nose NEC
	E06.2	Packing of anterior cavity of nose NEC
	E06.3	Removal of packing from cavity of nose
	E06.4	Balloon packing of cavity of nose
	E06.8	Other specified packing of cavity of nose
	E06.9	Unspecified packing of cavity of nose
	X56.1	Nasotracheal intubation
Haematology Procedures		
Blood transfusion/red cell or plasma exchange	X32	Exchange blood transfusion
	X32.1	Neonatal exchange blood transfusion
	X32.2	Exchange of plasma (single)

	X32.3	Exchange of plasma (2-9)
	X32.4	Exchange of plasma (10-19)
	X32.5	Exchange of plasma (>19)
	X32.6	Red cell exchange
	X32.7	Leucopheresis
	X32.8	Other specified exchange blood transfusion
	X32.9	Unspecified exchange blood transfusion
	X33	Other blood transfusion
	X33.1	Intra-arterial blood transfusion
	X33.2	Intravenous blood transfusion of packed cells
	X33.3	Intravenous blood transfusion of platelets
	X33.4	Autologous peripheral blood stem cell transplant
	X33.5	Syngeneic peripheral blood stem cell transplant
	X33.6	Allogeneic peripheral blood stem cell transplant
	X33.7	Autologous transfusion of red blood cells
	X33.8	Other specified other blood transfusion
	X33.9	Unspecified other blood transfusion
	X34	Other intravenous transfusion
	X34.1	Transfusion of coagulation factor
	X34.2	Transfusion of plasma NEC
	X34.3	Transfusion of serum NEC
	X34.4	Transfusion of blood expander
	X34.8	Other specified other intravenous transfusion
	X34.9	Unspecified other intravenous transfusion
Bone marrow puncture	W36.5	Diagnostic extraction of bone marrow NEC
	Y66.7	Harvest of bone marrow
Obstetric & gynae procedures		
Abortion/dilatation & curettage	Q10	Curettage of uterus
	Q10.1	Dilation of cervix uteri and curettage of products of conception from uterus
	Q10.2	Curettage of products of conception from uterus NEC
	Q10.3	Dilation of cervix uteri and curettage of uterus NEC
	Q10.8	Other specified curettage of uterus
	Q10.9	Unspecified curettage of uterus
	Q11	Other evacuation of contents of uterus
	Q11.1	Vacuum aspiration of products of conception from uterus NEC
	Q11.2	Dilation of cervix uteri and evacuation of products of conception from uterus NEC
	Q11.3	Evacuation of products of conception from uterus NEC
	Q11.4	Extraction of menses
	Q11.5	Vacuum aspiration of products of conception from uterus using rigid cannula
	Q11.6	Vacuum aspiration of products of conception from uterus using flexible cannula
	Q11.8	Other specified other evacuation of contents of uterus
	Q11.9	Unspecified other evacuation of contents of uterus
Vaginal delivery	R19	Breech extraction delivery
	R19.1	Breech extraction delivery with version
	R19.8	Other specified breech extraction delivery
	R19.9	Unspecified breech extraction delivery
	R20	Other breech delivery
	R20.1	Spontaneous breech delivery
	R20.2	Assisted breech delivery
	R20.8	Other specified other breech delivery
	R20.9	Unspecified other breech delivery
	R21	Forceps cephalic delivery
	R21.1	High forceps cephalic delivery with rotation
	R21.2	High forceps cephalic delivery NEC
	R21.3	Mid forceps cephalic delivery with rotation
	R21.4	Mid forceps cephalic delivery NEC
	R21.5	Low forceps cephalic delivery

	R21.8	Other specified forceps cephalic delivery
	R21.9	Unspecified forceps cephalic delivery
	R22	Vacuum delivery
	R22.1	High vacuum delivery
	R22.2	Low vacuum delivery
	R22.3	Vacuum delivery before full dilation of cervix
	R22.8	Other specified vacuum delivery
	R22.9	Unspecified vacuum delivery
	R23	Cephalic vaginal delivery with abnormal presentation of head at delivery without instrument
	R23.1	Manipulative cephalic vaginal delivery with abnormal presentation of head at delivery without instrument
	R23.2	Non-manipulative cephalic vaginal delivery with abnormal presentation of head at delivery without instrument
	R23.8	Other specified cephalic vaginal delivery with abnormal presentation of head at delivery without instrument
	R23.9	Unspecified cephalic vaginal delivery with abnormal presentation of head at delivery without instrument
	R24	Normal delivery
	R24.9	All normal delivery
Caesarean delivery	R17	Elective caesarean delivery
	R17.1	Elective upper uterine segment caesarean delivery
	R17.2	Elective lower uterine segment caesarean delivery
	R17.8	Other specified elective caesarean delivery
	R17.9	Unspecified elective caesarean delivery
	R18	Other caesarean delivery
	R18.1	Upper uterine segment caesarean delivery NEC
	R18.2	Lower uterine segment caesarean delivery NEC
	R18.8	Other specified other caesarean delivery
	R18.9	Unspecified other caesarean delivery
Skin Procedures		
Skin and wound management procedures	S41	Suture of skin of head or neck
	S41.1	Primary suture of skin of head or neck NEC
	S41.2	Delayed primary suture of skin of head or neck
	S41.3	Secondary suture of skin of head or neck
	S41.4	Resuture of skin of head or neck
	S41.8	Other specified suture of skin of head or neck
	S41.9	Unspecified suture of skin of head or neck
	S42	Suture of skin of other site
	S42.1	Primary suture of skin NEC
	S42.2	Delayed primary suture of skin NEC
	S42.3	Secondary suture of skin NEC
	S42.4	Resuture of skin NEC
	S42.8	Other specified suture of skin of other site
	S42.9	Unspecified suture of skin of other site
	S47	Opening of skin
	S47.1	Drainage of lesion of skin of head or neck
	S47.2	Drainage of lesion of skin NEC
	S47.3	Incision of lesion of skin of head or neck
	S47.4	Incision of lesion of skin NEC
	S47.5	Incision of skin of head or neck
	S47.6	Incision of skin NEC
	S47.8	Other specified opening of skin
	S47.9	Unspecified opening of skin
	S54	Exploration of burnt skin of head or neck
	S54.1	Debridement of burnt skin of head or neck
	S54.2	Removal of slough from burnt skin of head or neck
	S54.3	Toilet to burnt skin of head or neck NEC

	S54.4	Dressing of burnt skin of head or neck NEC
	S54.5	Attention to dressing of burnt skin of head or neck
	S54.6	Cleansing and sterilisation of burnt skin of head or neck
	S54.7	Dressing of burnt skin of head or neck using vacuum assisted closure device
	S54.8	Other specified exploration of burnt skin of head or neck
	S54.9	Unspecified exploration of burnt skin of head or neck
	S55	Exploration of burnt skin of other site
	S55.1	Debridement of burnt skin NEC
	S55.2	Removal of slough from burnt skin NEC
	S55.3	Toilet to burnt skin NEC
	S55.4	Dressing of burnt skin NEC
	S55.5	Attention to dressing of burnt skin NEC
	S55.6	Cleansing and sterilisation of burnt skin NEC
	S55.7	Dressing of burnt skin using vacuum assisted closure device NEC
	S55.8	Other specified exploration of burnt skin of other site
	S55.9	Unspecified exploration of burnt skin of other site
	S56	Exploration of other skin of head or neck
	S56.1	Debridement of skin of head or neck NEC
	S56.2	Removal of slough from skin of head or neck NEC
	S56.3	Toilet to skin of head or neck NEC
	S56.4	Dressing of skin of head or neck NEC
	S56.5	Attention to dressing of skin of head or neck NEC
	S56.6	Cleansing and sterilisation of skin of head or neck NEC
	S56.7	Dressing of skin of head or neck using vacuum assisted closure device NEC
	S56.8	Other specified exploration of other skin of head or neck
	S56.9	Unspecified exploration of other skin of head or neck
	S57	Exploration of other skin of other site
	S57.1	Debridement of skin NEC
	S57.2	Removal of slough from skin NEC
	S57.3	Toilet of skin NEC
	S57.4	Dressing of skin NEC
	S57.5	Attention to dressing of skin NEC
	S57.6	Cleansing and sterilisation of skin NEC
	S57.7	Dressing of skin using vacuum assisted closure device NEC
	S57.8	Other specified exploration of other skin of other site
	S57.9	Unspecified exploration of other skin of other site
Dental Procedures		
Extractions & surgical removal of teeth	F09	Surgical removal of tooth
	F09.1	Surgical removal of impacted wisdom tooth
	F09.2	Surgical removal of impacted tooth NEC
	F09.3	Surgical removal of wisdom tooth NEC
	F09.4	Surgical removal of tooth NEC
	F09.5	Surgical removal of retained root of tooth
	F09.8	Other specified surgical removal of tooth
	F09.9	Unspecified surgical removal of tooth
	F10	Simple extraction of tooth
	F10.1	Full dental clearance
	F10.2	Upper dental clearance
	F10.3	Lower dental clearance
	F10.4	Extraction of multiple teeth NEC
	F10.8	Other specified simple extraction of tooth
F10.9	Unspecified simple extraction of tooth	
Other oral surgical procedures	F01	Partial excision of lip
	F01.1	Excision of vermilion border of lip and advancement of mucosa of lip
	F01.8	Other specified partial excision of lip
	F01.9	Unspecified partial excision of lip
	F02	Extirpation of lesion of lip
F02.1	Excision of lesion of lip	

F02.2	Destruction of lesion of lip
F02.8	Other specified extirpation of lesion of lip
F02.9	Unspecified extirpation of lesion of lip
F03	Correction of deformity of lip
F03.1	Primary closure of cleft lip
F03.2	Revision of primary closure of cleft lip
F03.3	Adjustment to vermilion border of lip NEC
F03.8	Other specified correction of deformity of lip
F03.9	Unspecified correction of deformity of lip
F04	Other reconstruction of lip
F04.1	Reconstruction of lip using tongue flap
F04.2	Reconstruction of lip using skin flap
F04.8	Other specified other reconstruction of lip
F04.9	Unspecified other reconstruction of lip
F05	Other repair of lip
F05.1	Excision of excess mucosa from lip
F05.2	Advancement of mucosa of lip NEC
F05.3	Suture of lip
F05.4	Removal of suture from lip
F05.8	Other specified other repair of lip
F05.9	Unspecified other repair of lip
F06	Other operations on lip
F06.1	Division of adhesions of lip
F06.2	Biopsy of lesion of lip
F06.3	Shave of lip
F06.8	Other specified other operations on lip
F06.9	Unspecified other operations on lip
F08	Implantation of tooth
F08.1	Allotransplantation of tooth
F08.2	Autotransplantation of tooth
F08.3	Replantation of tooth
F08.4	Repositioning of tooth
F08.8	Other specified implantation of tooth
F08.9	Unspecified implantation of tooth
F11	Preprosthetic oral surgery
F11.1	Oral alveoplasty
F11.2	Augmentation of alveolar ridge using autobone graft
F11.3	Augmentation of alveolar ridge NEC
F11.4	Vestibuloplasty of mouth
F11.5	Endosseous implantation into jaw
F11.6	Subperiosteal implantation into jaw
F11.8	Other specified preprosthetic oral surgery
F11.9	Unspecified preprosthetic oral surgery
F18	Excision of dental lesion of jaw
F18.1	Enucleation of dental cyst of jaw
F18.2	Marsupialisation of dental lesion of jaw
F18.8	Other specified excision of dental lesion of jaw
F18.9	Unspecified excision of dental lesion of jaw
F22	Excision of tongue
F22.1	Total glossectomy
F22.2	Partial glossectomy
F22.8	Other specified excision of tongue
F22.9	Unspecified excision of tongue
F23	Extirpation of lesion of tongue
F23.1	Excision of lesion of tongue
F23.2	Destruction of lesion of tongue
F23.8	Other specified extirpation of lesion of tongue
F23.9	Unspecified extirpation of lesion of tongue

F24	Incision of tongue
F24.1	Biopsy of lesion of tongue
F24.2	Removal of foreign body from tongue
F24.3	Glossotomy
F24.8	Other specified incision of tongue
F24.9	Unspecified incision of tongue
F26	Other operations on tongue
F26.1	Commissurectomy of tongue
F26.2	Excision of frenulum of tongue
F26.3	Incision of frenulum of tongue
F26.4	Freeing of adhesions of tongue
F26.5	Suture of tongue
F26.8	Other specified other operations on tongue
F26.9	Unspecified other operations on tongue
F28	Extirpation of lesions of palate
F28.1	Excision of lesion of palate
F28.2	Destruction of lesion of palate
F28.8	Other specified extirpation of lesion of palate
F28.9	Unspecified extirpation of lesion of palate
F29	Correction of deformity of palate
F29.1	Primary repair of cleft palate
F29.2	Revision of repair of cleft palate
F29.8	Other specified correction of deformity of cleft palate
F29.9	Unspecified correction of deformity of palate
F30	Other repair of palate
F30.1	Plastic repair of palate using flap of palate
F30.2	Plastic repair of palate using flap of skin
F30.3	Plastic repair of palate using flap of tongue
F30.4	Plastic repair of palate using graft of skin
F30.5	Plastic repair of palate using flap of mucosa
F30.6	Plastic repair of palate using graft of mucosa
F30.7	Suture of palate
F30.8	Other specified other repair of palate
F30.9	Unspecified other repair of palate
F32	Other operations on palate
F32.1	Biopsy of lesion of palate
F32.2	Removal of foreign body from palate
F32.3	Incision of palate
F32.4	Operations on uvula NEC
F32.5	Uvulopalatopharyngoplasty
F32.6	Uvulopalatoplasty
F32.8	Other specified other operations on palate
F32.9	Unspecified other operations on palate
F38	Extirpation of lesion of other part of mouth
F38.1	Excision of lesion of floor of mouth
F38.2	Excision of lesion of mouth NEC
F38.3	Destruction of lesion of floor of mouth
F38.4	Destruction of lesion of mouth NEC
F38.8	Other specified extirpation of lesion of other part of mouth
F38.9	Unspecified extirpation of lesion of other part of mouth
F39	Reconstruction of other part of mouth
F39.1	Reconstruction of mouth using flap NEC
F39.2	Reconstruction of mouth using graft NEC
F39.8	Other specified reconstruction of other part of mouth
F39.9	Unspecified reconstruction of other part of mouth
F40	Other repair of other part of mouth
F40.1	Revision of repair of mouth NEC
F40.2	Graft of skin to mouth NEC

	F40.3	Graft of mucosa to mouth NEC
	F40.4	Suture of mouth NEC
	F40.5	Removal of suture from mouth NEC
	F40.8	Other specified other repair of other part of mouth
	F40.9	Unspecified other repair of other part of mouth
	F42.1	Biopsy of lesion of mouth NEC
	F42.2	Incision of mouth NEC
	F42.3	Removal of excess mucosa from mouth NEC
Endodontic procedures	F12	Surgery on apex of tooth
	F12.1	Apicectomy of tooth
	F12.2	Root canal therapy to tooth
	F12.8	Other specified surgery on apex of tooth
	F12.9	Unspecified surgery on apex of tooth
Scaling and gingival procedures	F16.4	Scaling of tooth
	F20	Operations on gingiva
	F20.1	Excision of gingiva
	F20.2	Excision of lesion of gingiva
	F20.3	Biopsy of lesion of gingiva
	F20.4	Gingivoplasty
	F20.5	Suture of gingiva
	F20.8	Other specified operations on gingiva
	F20.9	Unspecified operations on gingiva
Restorative Dental Procedures	F13.1	Full restoration of crown of tooth
	F13.2	Partial restoration of crown of tooth
	F13.3	Restoration of crown of tooth NEC
	F13.4	Restoration of part of using inlay NEC
	F13.5	Restoration of part of tooth using filling NEC
	F13.8	Other specified restoration of tooth
	F13.9	Unspecified restoration of tooth
	F17.1	Preparation of tooth for dental crown
	F17.6	Preparation of teeth for bridge

Note: * = endoscopic GI procedures treated as interventional in sub analysis of upper and lower GI endoscopic procedures, # = endoscopic GI procedures treated as non-interventional

Table S6. Case-crossover step-analysis comparing the incidence of invasive procedures (IPs) using a 4-month case period and preceding 11-month control period for 14,731 patients admitted with IE.

Invasive Procedures (IPs)	Case Period (4m)		Control Period (11m)		Unadjusted step model ^b		Adjusted step-model ^c		
	Total proc ^a	Proc/m ^a	Total proc ^a	Proc/m ^a	OR	95% CI	OR	95% CI	p-value
Cardiac Procedures									
Coronary angiography	465	116.3	892	81.1	1.44	1.28 to 1.61	0.97	0.81 to 1.16	0.897
Coronary artery bypass graft (CABG)	15	3.8	9	0.8	4.58	2.01 to 10.48	6.31	1.14 to 34.48	0.156
Percutaneous coronary procedures and stents	65	16.3	86	7.8	2.1	1.52 to 2.90	1.42	0.81 to 2.49	0.497
Implantation of cardiac pacemakers/defibrillators	547	136.8	588	53.5	2.6	2.32 to 2.93	1.29	1.05 to 1.58	0.086
Percutaneous valve procedures	9	2.3	29	2.6	0.85	0.40 to 1.81	1.15	0.35 to 3.72	0.895
Dental Procedures									
Extractions or surgical removal of teeth	69	17.3	66	6	2.89	2.06 to 4.05	3.35	1.75 to 6.39	0.021
Other oral surgical procedures	14	3.5	24	2.2	1.61	0.83 to 3.13	0.84	0.29 to 2.46	0.865
Scaling and gingival procedures	1	0.3	1	0.1	2.75	0.17 to 43.90	1.06	0.01 to 126.76	0.981
ENT procedures									
Tonsillectomy & Adenoidectomy	3	0.8	5	0.5	1.65	0.39 to 6.90	0.31	0.03 to 2.95	0.588
Nasal packing/nasal intubation	33	8.3	49	4.5	1.93	1.22 to 3.04	1.03	0.48 to 2.02	0.979
GI Procedures									
Upper GI endoscopic procedures (gastric, duodenum, jejunum, ileum)	754	188.5	887	80.6	2.43	2.20 to 2.69	1.43	1.20 to 1.69	0.007
Lower GI endoscopic procedures (including sigmoid and rectum)	412	103	577	52.5	2	1.76 to 2.27	1.69	1.35 to 2.12	0.010
Colonic surgery (incl appendix)	33	8.3	54	4.9	1.68	1.09 to 2.59	1.15	0.56 to 2.36	0.910
Endoscopic Retrograde Cholangio-pancreatic Procedures (ERCP)	35	8.8	47	4.3	2.13	1.36 to 3.35	1.42	0.65 to 3.07	0.577
GU Procedures									
Cystoscopic procedures	204	51	452	41.1	1.27	1.07 to 1.51	0.9	0.69 to 1.19	0.670
Endoscopic prostate procedures	53	13.3	93	8.5	1.57	1.12 to 2.21	0.59	0.35 to 1.02	0.222

Haematology Procedures									
Blood transfusion/red cell or plasma exchange	368	92	587	53.4	2.7	2.26 to 3.24	1.15	0.86 to 1.54	0.633
Bone marrow puncture	114	28.5	129	11.7	2.58	1.99 to 3.35	1.29	0.82 to 2.02	0.562
Obstetric & gynaecological procedures									
Abortion/dilatation & curettage	5	1.3	10	0.9	1.38	0.47 to 4.07	1.66	0.27 to 10.32	0.797
Vaginal delivery	8	2	28	2.5	0.79	0.36 to 1.72	0.59	0.19 to 1.86	0.611
Caesarean delivery	5	1.3	7	0.6	1.96	0.62 to 6.19	10.86	0.84 to 140.64	0.223
Respiratory Procedures									
Bronchoscopic procedures	60	15	63	5.7	2.65	1.86 to 3.79	1.63	0.87 to 3.05	0.374
Skin Procedures									
Skin and wound management procedures	134	33.5	268	24.4	1.39	1.12 to 1.71	0.78	0.56 to 1.09	0.355

Notes: a, a maximum of one procedure of each type per patient was counted each month. b, period-adjusted OR of IPs in case period (4 months prior to IE admission) compared to control period (15 to 5 months prior to IE admission) calculated using a mixed effects logistic regression model with the patient as the random effect. c, OR of IPs in case period (4 months prior to IE admission) compared to control period (15 to 5 months prior to IE admission) calculated using a mixed effects logistic regression model adjusted for month and date of IE admission with the patient as the random effect. m=month, proc=procedures, OR=odds ratio, CI=confidence interval, IE=infective endocarditis, IPs=invasive procedures. **P values in red** = significant positive association between the IP and subsequent IE following Benjamini-Hochberg correction. **P values in purple** = significant negative association between IP and subsequent IE following Benjamini-Hochberg correction.

Table S7. Case-crossover step-analysis comparing the incidence of invasive procedures (IPs) using a 6-month case period and preceding 9-month control period for 14,731 patients admitted with IE.

Invasive Procedures (IPs)	Case Period (4m)		Control Period (11m)		Unadjusted step model ^b		Adjusted step-model ^c		
	Total proc ^a	Proc/m ^a	Total proc ^a	Proc/m ^a	OR	95% CI	OR	95% CI	p-value
Cardiac Procedures									
Coronary angiography	656	109.3	701	77.9	1.41	1.26 to 1.57	0.86	0.70 to 1.06	0.909
Coronary artery bypass graft (CABG)	15	2.5	9	1	2.5	1.09 to 5.72	0.62	0.12 to 3.12	0.806
Percutaneous coronary procedures and stents	81	13.5	70	7.8	1.75	1.27 to 2.41	0.74	0.40 to 1.39	1.000
Implantation of cardiac pacemakers/defibrillators	702	117	433	48.1	2.47	2.19 to 2.79	0.98	0.78 to 1.24	0.878
Percutaneous valve procedures	12	2	26	2.9	0.69	0.34 to 1.37	0.59	0.17 to 2.04	0.718
Dental Procedures									
Extractions or surgical removal of teeth	80	13.3	55	6.1	2.19	1.55 to 3.09	1.37	0.69 to 2.69	0.940
Other oral surgical procedures	20	3.3	18	2	1.68	0.88 to 3.18	0.86	0.25 to 2.99	0.930
Scaling and gingival procedures	1	0.2	1	0.1	1.5	0.09 to 23.94	0.08	0.00 to 27.91	0.755
ENT procedures									
Tonsillectomy & Adenoidectomy	5	0.8	3	0.3	2.5	0.60 to 10.46	0.77	0.05 to 12.62	0.894
Nasal packing/nasal intubation	43	7.2	39	4.3	1.71	1.09 to 2.67	0.61	0.26 to 1.45	0.874
GI Procedures									
Upper GI endoscopic procedures (gastric, duodenum, jejunum, ileum)	972	162	669	74.3	2.25	2.04 to 2.49	1.07	0.88 to 1.31	0.747
Lower GI Endoscopic procedures (including sigmoid and rectum)	510	85	479	53.2	1.62	1.42 to 1.83	0.86	0.67 to 1.09	0.980
Colonic surgery (incl appendix)	43	7.2	44	4.9	1.47	0.96 to 2.23	0.69	0.31 to 1.56	0.860
Endoscopic Retrograde Cholangio-pancreatic Procedures (ERCP)	46	7.7	36	4	1.98	1.27 to 3.10	1.13	0.47 to 2.73	0.947
GU Procedures									
Cystoscopic procedures	313	52.2	343	38.1	1.41	1.20 to 1.66	1.27	0.93 to 1.74	1.000
Endoscopic prostate procedures	86	14.3	60	6.7	2.17	1.55 to 3.02	1.48	0.77 to 2.85	0.924

Haematology Procedures									
Blood transfusion/red cell or plasma exchange	503	83.8	452	50.2	2.54	2.13 to 3.02	0.88	0.63 to 1.23	0.731
Bone marrow puncture	149	24.8	94	10.4	2.51	1.92 to 3.27	1.1	0.65 to 1.86	0.912
Obstetric & gynaecological procedures									
Abortion/dilatation & curettage	6	1	9	1	1	0.35 to 2.83	0.62	0.09 to 4.29	0.846
Vaginal delivery	11	1.8	25	2.8	0.66	0.32 to 1.34	0.26	0.08 to 0.91	0.805
Caesarean delivery	6	1	6	0.7	1.5	0.48 to 4.65	6.15	0.51 to 74.18	1.000
Respiratory Procedures									
Bronchoscopic procedures	74	12.3	49	5.4	2.29	1.59 to 3.29	0.93	0.46 to 1.90	0.932
Skin Procedures									
Skin and wound management procedures	207	34.5	195	21.7	1.61	1.32 to 1.96	1.19	0.80 to 1.75	0.815

Notes: a, a maximum of one procedure of each type per patient was counted each month. b, period-adjusted OR of IPs in case period (6 months prior to IE admission) compared to control period (15 to 7 months prior to IE admission) calculated using a mixed effects logistic regression model with the patient as the random effect. c, OR of IPs in case period (6 months prior to IE admission) compared to control period (15 to 7 months prior to IE admission) calculated using a mixed effects logistic regression model adjusted for month and date of IE admission with the patient as the random effect. m=month, proc=procedures, OR=odds ratio, CI=confidence interval, IE=infective endocarditis, IPs=invasive procedures. **P values in red** = significant positive association between the IP and subsequent IE following Benjamini-Hochberg correction. **P values in purple** = significant negative association between IP and subsequent IE following Benjamini-Hochberg correction.

Figure S1. Incidence of different invasive procedures (IPs) over the 15 months before infective endocarditis (IE) hospital admission.



Figure S1. Continued.



Notes: ENT = Ear, nose and throat, GI = gastrointestinal, GU = genitourinary, IE = infective endocarditis, Obs & Gynae = Obstetrics and gynaecology, Procs = procedures. Cyan bars represent the control-period (months -4 to -15). Magenta bars represent the case-period (months -1 to -3), IE admission - day zero.

References:

- 1 Ramsdale DR, Turner-Stokes L, Advisory Group of the British Cardiac Society Clinical Practice C, et al. Prophylaxis and treatment of infective endocarditis in adults: a concise guide. *Clin Med (Lond)* 2004;**4**:545-50.
- 2 Horstkotte D, Follath F, Gutschik E, et al. Guidelines on prevention, diagnosis and treatment of infective endocarditis executive summary; the task force on infective endocarditis of the European society of cardiology. *Eur Heart J* 2004;**25**:267-76.
- 3 Dajani AS, Taubert KA, Wilson W, et al. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. *JAMA* 1997;**277**:1794-801.
- 4 Janszky I, Gemes K, Ahnve S, et al. Invasive Procedures Associated With the Development of Infective Endocarditis. *J Am Coll Cardiol* 2018;**71**:2744-52.
- 5 Habib G, Hoen B, Tornos P, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Society of Chemotherapy (ISC) for Infection and Cancer. *Eur Heart J* 2009;**30**:2369-413.
- 6 Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation* 2007;**116**:1736-54.
- 7 National Institute for Health and Care Excellence (NICE). Prophylaxis against infective endocarditis. Clinical Guideline [CG64]. National Institute for Health and Care Excellence (NICE) 2008:NICE Clinical Guideline No 64.