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Thornhill, M. orcid.org/0000-0003-0681-4083, Crum, A., Campbell, R. et al. (9 more authors) (2023) Temporal association between invasive procedures and infective endocarditis. Heart, 109 (3). pp. 223-231. ISSN 1355-6037

https://doi.org/10.1136/heartjnl-2022-321519

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Original research

# Temporal association between invasive procedures and infective endocarditis

**OPEN ACCESS** 

Ellen C Lee,<sup>3</sup> Mike Bradburn,<sup>4</sup> Veronica Fibisan,<sup>3</sup> Mark Dayer 💿 ,<sup>5</sup> Bernard D Prendergast 💿 ,<sup>6</sup> Peter Lockhart,<sup>2</sup> Larry Baddour 💿 ,<sup>7</sup> Jon Nicoll<sup>3</sup>  $\sim$ Martin H Thornhill 💿 ,<sup>1,2</sup> Annabel Crum,<sup>3</sup> Richard Campbell,<sup>3</sup> Tony Stone,

## ABSTRACT

Additional supplemental

material is published online

only. To view, please visit the

journal online (http://dx.doi. org/10.1136/heartjnl-2022-

321519).

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

<sup>1</sup>Department of Oral & Maxillofacial Medicine, Surgery

and Pathology, The University of Sheffield School of Clinical

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

Research, Sheffield, UK <sup>4</sup>CTRU, University of Sheffield School of Health and Related

School of Health and Related

<sup>3</sup>The University of Sheffield

Thomas' Hospital, London, UK <sup>7</sup>Departments of Medicine and

<sup>6</sup>Department of Cardiology, St

Taunton, Somerset, UK

'Department of Cardiology, Somerset Foundation Trust,

Research, Sheffield, UK

Clinic College of Medicine and Science, Rochester, Minnesota,

USA

Cardiovascular Disease, Mayo

Charlotte, North Carolina, USA

<sup>2</sup>Department of Oral Medicine/

Dentistry, Sheffield, UK

Oral & Maxillofacial Surgery,

Carolinas Medical Center,

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 association between specific IPs (permanent pacemaker an alternative analysis, bronchoscopy (OR 1.33, 95% CI (OR 1.54, 95% CI 1.27 to 1.85, p<0.001), extractions/ surgical tooth removal (OR 2.14, 95% Cl 1.22 to 3.76, p=0.047), upper (OR 1.58, 95% Cl 1.34 to 1.85, permanent pacemaker and defibrillator implantation subsequent IE that warrants re-evaluation of current p<0.001) and lower gastrointestinal endoscopy (OR cell/plasma exchange (OR 1.2, 95% CI 1.07 to 1.35, and defibrillator implantation, dental extraction, gastrointestinal endoscopy and bronchoscopy) and 1.06 to 1.68, p=0.049) and blood transfusions/red Results The odds of IE were increased following **Conclusions** This study identifies a significant p=0.012) were also associated with IE.

antibiotic prophylaxis recommendations to prevent IE in high IE risk individuals.

Dentistry, Sheffield, Sheffield, UK; m.thornhill@sheffield.ac.uk

Received 15 June 2022 Accepted 2 September 2022

Maxillofacial Medicine, Surgery and Pathology, The University of Sheffield School of Clinical

Dr Martin H Thornhill, Oral &

Correspondence to

# INTRODUCTION

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and Infective endocarditis (IE) incidence has increased implantable cardioverter-defibrillators, surgical and transcatheter heart valves), vascular interventions (including haemodialysis), injection drug use, greater IE awareness and access to investigations (especially the rest of Europe.<sup>2</sup> Responsible factors could an ageing population, increased intrasignificantly in the last decade in the UK<sup>1</sup> device use (pacemakers, include cardiac

# WHAT IS ALREADY KNOWN ON THIS TOPIC

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

# WHAT THIS STUDY ADDS

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

# HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

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

echocardiography), and changes in IE prevention guidelines.

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





*et al. Heart* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/

To cite: Thornhill MH,

Crum A, Campbell R,

heartjnl-2022-321519



### 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.<sup>7 8 11 12</sup> 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.<sup>7</sup> 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).<sup>4 5</sup>

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)<sup>6</sup> and before any relaxation of this (April 2016).<sup>9</sup> Thus, any association between IPs and IE should have been fully exposed.

#### Case-crossover study

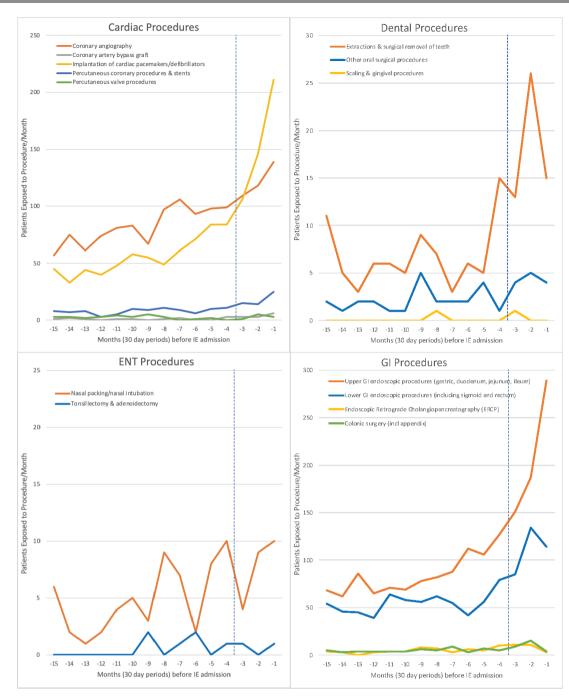
#### Primary analysis

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,<sup>10</sup> 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.<sup>11</sup>

#### 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

#### Valvular heart disease



**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

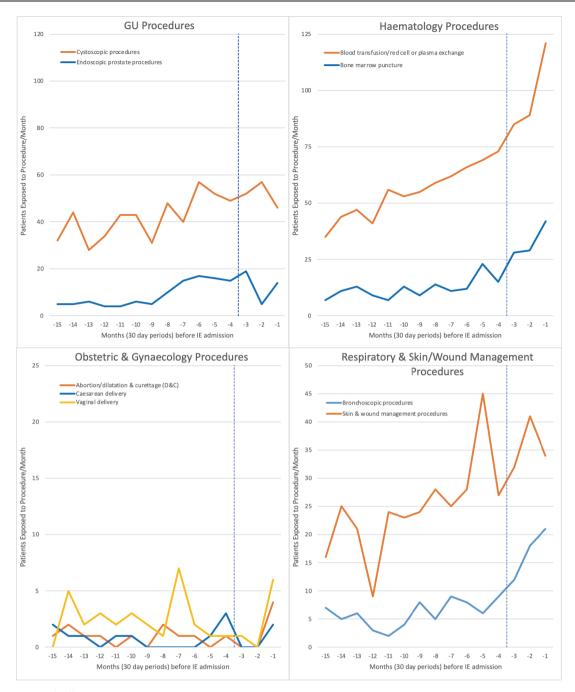
Attributable risk (or absolute risk increase) was defined as the additional number of IE cases per 100 000 procedures) and was estimated for IPs with a significant positive association with IE. The background IE incidence was estimated by dividing the total number of IE cases identified during the study 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 × (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).<sup>12</sup> <sup>13</sup>

#### RESULTS

#### Study population demographics

Between 1 April 2010 and 31 March 2016, there were 14731 IE admissions (mean age 62.3 years, 66.1% male) in England



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**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 14731 patients admitted with IE

	Case period Control period (3 m) (12 m)		iod	Unadjusted step model† Adj		Adju	Adjusted step model‡		Adju	Adjusted hinge model§		
	Total											Р
Invasive procedures (ISPs)	proc*	Proc/m*	Total proc*	Proc/m*	OR	95% <b>CI</b>	OR	95% <b>CI</b>	P value	OR	95% <b>CI</b>	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	<0.00
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	<0.00
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	< 0.00
Colonic surgery (including appendicectomy)	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.

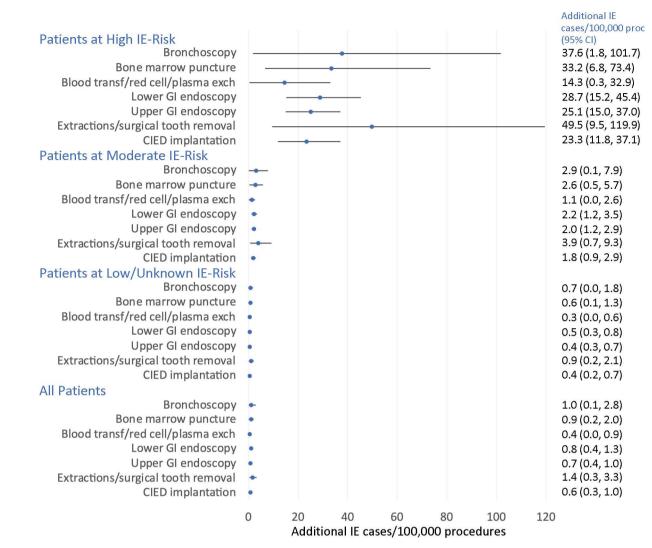
neither statistically nor clinically significant, comprising small effects (OR below 1.05) and/or infrequent procedures (<10 per month in control periods).

(figure 3). The absolute risk was greatest for those at high IE

For IPs with evidence of an association with IE, the absolute risk increase (attributable risk) was small for low/unknown risk DISCUSSION and moderate risk patients, with estimated attributable risk below 1 per 100000 procedures for those at low/unknown IE risk and below 4 per 100000 for those at moderate IE risk

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).

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 100000 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 100000 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 devises; 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.<sup>14 15</sup> 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.<sup>8</sup> 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.<sup>16 17</sup> Nonetheless, there was considerable variation in the AP regimens used.<sup>16 17</sup> Concerns about this led to the first UK CIED infection prevention guidelines in 2015.<sup>18</sup> The incidence of IE following CIED insertion has been calculated at 550 cases/million procedures per year.<sup>19</sup> 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,<sup>18</sup> 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.<sup>20</sup>

#### **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%

rectum) GI endoscopic procedures and IE. The increase in attrib-
utable risk was, respectively, 25.1 and 28.7 per 100000 proce-
dures for those at high IE risk undergoing upper or lower GI
endoscopy and 2.0 and 2.2 per 100000 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 endoscopy 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.<sup>8</sup>

Two case series have identified IE following endoscopy,<sup>22 23</sup> and elevated IE incidence has been noted in elderly high IE risk patients following colonoscopy.<sup>24</sup> 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.<sup>25</sup> 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.<sup>26</sup>

#### 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).<sup>8</sup>

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 study<sup>8</sup> identified an association between bronchoscopy and subsequent IE. Furthermore, our attributable risk estimate was 38 additional IE cases per 100000 procedures for those at high IE risk. Bacteraemia is a recognised complication of bronchoscopy.<sup>27</sup> Nonetheless, consistent with NICE guidance,<sup>20</sup> current British Thoracic Society guidelines recommend against the use of AP to prevent IE in those undergoing flexible bronchoscopy.<sup>28</sup>

#### 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.

Characteristics	Statistics	All IE admissions
Age	Ν	14722
	Mean (SD)	62.3 (19.9)
	Median (min, max)	67.0 (0, 103)
Sex	Ν	14731
	Male, n (%)	9734 (66.1)
	Female, n (%)	4997 (33.9)
Level of IE risk	Ν	14731
before admission	High risk, n (%)	3145 (21.3)
	Moderate risk, n (%)	2503 (17.0)
	Low/unknown risk, n (%)	9083 (61.7)
Reason for high-	Previous IE, n (%)	154 (4.9)
risk stratification*	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	Previous rheumatic fever, n (%)	808 (32.3)
moderate-risk	Non-rheumatic valve disease, n (%)	1571 (62.8)
stratification*	Congenital valve anomalies, n (%)	58 (2.3)
	Hypertrophic cardiomyopathy, n (%)	66 (2.6)
Admission date	Ν	14731
	Min	01 Apr 2010
	Max	28 Mar 2016
Discharge date	Ν	14297
	Min	6 April 2010
	Max	31 March 2016
Hospital length of	Ν	14297
stay (days)*	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)

Autough we excluded patients discharged anve 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.

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 0000 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.<sup>21</sup> 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.<sup>9 14 15</sup>

#### GI procedures

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

#### Valvular heart disease

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,<sup>8</sup> 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,<sup>29</sup> 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.<sup>8</sup> 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.<sup>10</sup> 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).<sup>7</sup> 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.<sup>30</sup>

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/100000 procedures in those at high IE risk and an additional 1.1–3.9 IE cases/100000 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.

**Funding** This work was supported by a British Heart Foundation Project Grant (PG/20/10410).

**Competing interests** MHT, AC, RC, TS, ECL, MB, VF and JN all received salary support from the British Heart Foundation (Project Grant PG/20/10410) for this study. MHT, PL and JN report other grant support from the National Institutes for Health (USA) or the National Institute for Health Research (UK). BDP reports unrestricted educational and research grants from Edwards Lifesciences, and personal speaker/consultancy fees from Medtronic, Abbott, Microport, Anteris and Edwards Lifesciences. LB reports consulting for Boston Scientific and Roivant Sciences, and royalty payments from UpToDate, Inc. MD reports payment for expert testimony from Bevan Brittan, honoraria for presentations and support for attending meetings from Biotronik. JN reports being chair of the REPHILL trial data monitoring committee from (National Institute for Health and Care Research (NIHR)), chair of research commissioning panels for COVID research (CSO Scotland), member of the UKRI-DHSC COVID-19 Vaccine trial commissioning panel and member of the NIHR commissioning panel for emergency care procedures research.

**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.

Provenance and peer review Not commissioned; externally peer reviewed.

**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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#### ORCID iDs

Martin H Thornhill http://orcid.org/0000-0003-0681-4083 Mark Dayer http://orcid.org/0000-0002-0976-9743 Bernard D Prendergast http://orcid.org/0000-0002-6031-2124 Larry Baddour http://orcid.org/0000-0002-4473-7077

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#### **Supplementary Appendix**

#### Temporal Association Between Invasive Procedures and Infective Endocarditis

#### **Brief Title – Endocarditis and invasive procedures**

Martin H. Thornhill, MBBS, BDS, PhD<sup>a,b</sup>, Annabel Crum, BSc<sup>c</sup>, Richard Campbell, MPH<sup>c</sup>, Ellen C. Lee BSC, <sup>M.Scc</sup>, Veronica Fibisan PhD<sup>c</sup>, Mark J. Dayer, MBBS, PhD<sup>d</sup>, Bernard D. Prendergast, BM, BS, DM<sup>e</sup>, Peter B. Lockhart, DDS<sup>b</sup>, Larry M. Baddour, MD<sup>g</sup>, Jon Nicholl, DSc<sup>c</sup>.

<sup>a</sup>Unit of Oral & Maxillofacial Medicine Surgery and Pathology, School of Clinical Dentistry, University of Sheffield, Sheffield, UK; <sup>c</sup>School of Health and Related Research, University of Sheffield, Sheffield, UK; <sup>b</sup>Department of Oral Medicine, Carolinas Medical Center – Atrium Health, Charlotte, NC; <sup>c</sup>IBM Watson Health, Ann Arbor, MI; <sup>d</sup>Department of Cardiology, Somerset Foundation Trust, Taunton, Somerset, UK; <sup>e</sup>Department of Cardiology, St Thomas' Hospital, London, UK; <sup>f</sup>Cardiovascular Medicine Division, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA; <sup>g</sup>Division of Infectious Diseases, Mayo Clinic College of Medicine and Science, Rochester, MN.

#### **Correspondence to:**

Prof. Martin Thornhill, Unit of Oral & Maxillofacial Medicine Surgery and Pathology, University of Sheffield School of Clinical Dentistry, Claremont Crescent, Sheffield S10 2TA, UK. Tel: +44 (0)751-555-2925, Email: <u>m.thornhill@sheffield.ac.uk</u>

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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:

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

Where  $p_{it}$  denotes the probability that the *i*<sup>th</sup> 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,  $\beta_{case}$  is the coefficient (log-odds) for the procedure in the case period compared to the non-case period,  $\gamma_i$  is a Normally distributed random effect  $\gamma_i$  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 "stepmodel"). 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:

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

Where  $d_t$  is the calendar date (1<sup>st</sup> April 2010 to 31<sup>st</sup> March 2016),  $\beta_{time}$  is the coefficient (log-odds) for the temporal association, and  $p_{it}$ ,  $I_{(l)}$  and  $\gamma_i$  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.

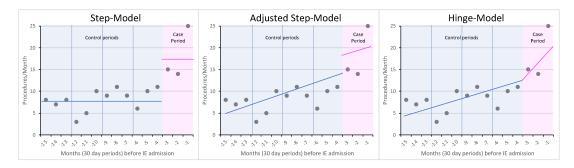
An alternative approach is to consider the slope of the IP incidence in the case- and controlperiods as continuous (i.e., without a step change) but with a change of slope (or trajectory) occurring at the point of transition from the control- to the case-period (i.e., with a hinge point in the slope). 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:

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

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			Janszky et al. 2018 <sup>4</sup>
GI Procedures	2004[1]	ESC 2004 <sup>2</sup>	AHA 1997 <sup>3</sup>	Inpatient IPs RR (95% CI)
Upper GI Endoscopy with/without biopsy	$\checkmark$	-	à	3.97 (2.68-5.88)
Lower GI Endoscopy with/without biopsy	$\checkmark$	-	à	2.82 (1.42-5.61)
ERCP (Endoscopic Retrograde Cholangio- Pancreatography)	$\checkmark$	$\checkmark$	$\checkmark$	3.60 (1.34-9.70)
Colonic Surgery	$\checkmark$	-	$\checkmark$	-
GU Procedures				
Endoscopic prostate procedures	$\checkmark$	$\checkmark$	$\checkmark$	-
Cystoscopy and endoscopic urological procedures	$\checkmark$	$\checkmark$	$\checkmark$	4.40 (1.67-11.62)
Obstetric & Gynaecological Procedures				
Caesarean section	$\checkmark$	-	-	-
Vaginal delivery	$\checkmark$	√§	à	-
Abortion/dilatation and curettage (D&C)	$\checkmark$	√§	-	3.00 (1.81-4.98)
Respiratory Procedures		·		·
Bronchoscopic procedures (esp. rigid)	$\checkmark$	$\checkmark$	$\checkmark$	16.00 (2.12-120.65)
Cardiac Procedures	•		•	
Implantation of pacemakers/defibrillators	$\checkmark$	-	-	9.75 (3.48-27.28)
Percutaneous valve procedures	$\checkmark$	-	-	-
Percutaneous coronary procedures/stents	$\checkmark$	-	-	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	$\checkmark$	$\checkmark$	$\checkmark$	2.33 (0.60-9.02)
Nasal packing/nasal intubation	$\checkmark$	-	-	-
Dermatological Procedures	·			
Skin suturing, drainage or wound management	$\checkmark$	-	-	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	$\checkmark$	$\checkmark$	$\checkmark$	-
Other oral surgical procedures	$\checkmark$	$\checkmark$	$\checkmark$	-
Scaling of teeth	$\checkmark$	$\checkmark$	$\checkmark$	-
Endodontic treatment	$\checkmark$	√	$\checkmark$	-

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,  $\checkmark$  = antibiotic prophylaxis recommended,  $\checkmark$ † = prophylaxis recommended as optional for high-risk patients,  $\checkmark$ § = 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	ICD-10 Diagnosis Codes and OPCS-4 Procedure codes
Condition	For Identifying Those at High-Risk of IE <sup>1</sup>
Previous IE	ICD-10 Diagnosis Codes:
	I330 Acute and subacute infective endocarditis
	1339 Acute endocarditis, unspecified
	I38X Endocarditis, valve unspecified
	1390 Endocarditis and mitral valve disorders in disease classified elsewhere
	I391 Endocarditis and aortic valve disorders in disease classified elsewhere
	1392 Endocarditis and tricuspid valve disorders in disease classified elsewhere
	1393 Endocarditis and pulmonary valve disorders in disease classified elsewhere
	1394 Endocarditis and multiple valve disorders in disease classified elsewhere
	1398 Endocarditis, valve unspecified in disease classified elsewhere
	B376 Candidal endocarditis
	T826 Infection and inflammatory reaction due to cardiac valve prosthesis
Prosthetic	OPCS-4 Procedure Codes:
replacement of	K251 Allograft replacement of mitral valve
heart 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
Valve repair	OPCS-4 Procedure Codes:
using prosthetic	K255 Mitral valve repair NEC
material	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

	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
Prosthetic heart	OPCS-4 Procedure Codes:
or ventricular	K023 Implantation of prosthetic heart
assist device	K025 Revision of implantation of prosthetic heart
assist device	K541 Open implantation of ventricular assist device
Congenital Heart	OPCS-4 Procedure Codes:
Condition (CHC)	K041 Repair of tetralogy of Fallot using valved right ventricular outflow conduit
. ,	K042 Repair of tetralogy of Fallot using right ventricular outflow conduit NEC
in whom a	K063 Left ventricle to aorta tunnel with right ventricle to pulmonary artery valved conduit
palliative shunt	K171 Total cavopulmonary connection with extracardiac inferior caval vein to pulmonary
or conduit has	artery conduit
been used	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 porta
	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 years ava
	K195 Creation of conduit between left ventricle of heart and vena cava
	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
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	L052 Creation of shunt to right pulmonary artery from ascending aorta using interposition
	tube prosthesis
	L053 Creation of shunt to left pulmonary artery from ascending aorta using interposition
	tube prosthesis
	L054 Percutaneous transluminal balloon dilatation of interposition tube prosthesis between pulmonary artery and aorta
	L058 Other specified creation of shunt to pulmonary artery from aorta using interposition
	tube prosthesis
	L059 Unspecified creation of shunt to pulmonary artery from aorta using interposition
	tube prosthesis
	L071 Creation of shunt to right pulmonary artery from right subclavian artery using
	interposition tube prosthesis
	L072 Creation of shunt to left pulmonary artery from left subclavian artery using
	interposition tube prosthesis
	L074 Percutaneous transluminal balloon dilatation of interposition tube prosthesis
	between pulmonary artery and subclavian artery
	L078 Other specified creation of shunt to pulmonary artery from subclavian artery using
	interposition tube prosthesis L079 Unspecified creation of shunt to pulmonary artery from subclavian artery using
	interposition tube prosthesis
Unrepaired	ICD-10 Diagnosis Codes:
cyanotic	Q200 Common arterial trunk
congenital heart	Q201 Double outlet right ventricle
condition $(CHC)^2$	Q202 Double outlet left ventricle
condition (on o)	Q203 Discordant ventriculoarterial connection
	Q204 Double inlet ventricle
	Q205 Discordant atrioventricular connection
	Q212 Atrioventricular septal defect
	Q213 Tetralogy of Fallot
	Q214 Aortopulmonary septal defect
Completely	Q262 Total anomalous pulmonary venous connection
Completely	OPCS-4 Procedure Codes:
repaired CHC	K091 Repair of defect of atrioventricular septum using dual prosthetic patches K092 Repair of defect of atrioventricular septum using prosthetic patch NEC
defect with	K101 Repair of defect of interatrial septum using prosthetic patch
prosthetic	K111 Repair of defect of interventricular septum using prosthetic patch
material or	K117 Repair of defect of inter ventricular septal defect using intraoperative transluminal
device, whether	prosthesis
placed by	K121 Repair of defect of septum of heart using prosthetic patch NEC
surgery or	K131 Percutaneous transluminal repair of defect of interventricular septum using
catheter	prosthesis
intervention,	K132 Percutaneous transluminal repair of defect of interventricular septum NEC
during first 6	K133 Percutaneous transluminal repair of defect of interatrial septum using prosthesis
months after the	K134 Percutaneous transluminal repair of defect of interatrial septum NEC K135 Percutaneous transluminal repair of defect of unspecified septum using prosthesis
procedure only. <sup>3</sup>	K138 Other specified transluminal repair of defect of interatrial septum
	K139 Unspecified transluminal repair of defect of interatrial septem
	K163 Percutaneous transluminal atrial septum fenestration closure with prosthesis
	K165 Percutaneous transluminal closure of patent oval foramen with prosthesis
	L031 Percutaneous transluminal prosthetic occlusion of patent ductus arteriosus
	L101 Repair of pulmonary artery using prosthesis
	L233 Plastic repair of aorta using patch graft

#### 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 <sup>1</sup>
Previous Rheumatic Fever	ICD-10 Diagnosis Codes:
	I011 Acute rheumatic endocarditis
	1018 Other acute rheumatic heart disease
	1019 Acute rheumatic heart disease, unspecified
	1020 Rheumatic chorea with heart involvement
	1050 Rheumatic mitral stenosis
	1051 Rheumatic mitral insufficiency
	1052 Rheumatic mitral stenosis with insufficiency
	1058 Other mitral valve disease
	1059 Rheumatic mitral valve disease, unspecified
	1060 Rheumatic aortic stenosis
	1061 Rheumatic aortic insufficiency
	1062 Rheumatic aortic stenosis with insufficiency
	1068 Other rheumatic aortic valve disease
	1069 Rheumatic aortic valve disease, unspecified
	1070 Rheumatic tricuspid stenosis
	1071 Rheumatic tricuspid insufficiency
	1072 Rheumatic tricuspid stenosis with insufficiency
	I078 Other rheumatic tricuspid valve disease I079 Rheumatic tricuspid valve disease, unspecified
	1080 Disorders of both mitral and aortic valves
	1081 Disorders of both mitral and tricuspid valves
	1082 Disorders of both aortic and tricuspid valves
	1083 Combined disorders of mitral, aortic and tricuspid valves
	1088 Other multiple valve disease
	1089 Multiple valve diseases, unspecified
	1090 Rheumatic myocarditis
	1091 Rheumatic disease of the endocardium, valve unspecified
	1098 Other specified rheumatic heart disease
	1099 Rheumatic heart disease, unspecified
Non-Rheumatic Valve	ICD-10 Diagnosis Codes:
Disease	1340 Mitral valve insufficiency
	I341 Mitral valve prolapse
	1342 Nonrheumatic mitral valve stenosis
	1348 Other nonrheumatic mitral valve disorders
	1349 Nonrheumatic mitral valve disorder, unspecified
	1350 Aortic valve stenosis
	I351 Aortic valve insufficiency
	1352 Aortic valve stenosis with insufficiency
	1358 Other nonrheumatic aortic valve disorders
	1359 Nonrheumatic aortic valve disorder, unspecified
	1360 Tricuspid valve stenosis
	1361 Tricuspid valve insufficiency
	I362 Tricuspid valve stenosis with insufficiency I368 Other nonrheumatic tricuspid valve disorders
	1369 Nonrheumatic tricuspid valve disorders
	I370 Pulmonary valve stenosis
	I371 Pulmonary valve insufficiency
	I372 Pulmonary valve stenosis with insufficiency
	1378 Other nonrheumatic pulmonary valve disorders
	1379 Nonrheumatic pulmonary valve disorder, unspecified

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 stenosisQ222 Congenital pulmonary valve insufficiencyQ223 Other congenital malformations of pulmonary valveQ224 Congenital tricuspid valve stenosisQ225 Ebstein anomalyQ228 Other congenital malformations of tricuspid valveQ229 Congenital malformations of tricuspid valve, unspecifiedQ230 Congenital stenosis of aortic valveQ231 Congenital insufficiency of aortic valveQ232 Congenital mitral valve stenosisQ233 Congenital mitral valve insufficiencyQ238 Other congenital malformations of aortic and mitral valvesQ239 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)	
<ul> <li>Transoesophageal echocardiography (TOE)</li> </ul>		U20.2	
<ul> <li>Oesophageal endoscopic procedures (excluding TOE)</li> </ul>		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)	
Peopiratory Presedures			
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 developin	a IE within 3	3 months of this procedure being performed ac	cording to the data

\* 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 S5Individual OPCS-4 Invasive Procedure (IPs) Code Descriptions

Procedure	Code	OPCS-4 Code Description
Cardiac Procedures		
Coronary angiography	K63	Contrast radiology of heart
	K63.1	Angiocardiography of combination of right and left side of heart
	K63.2	Angiocardiography of right side of heart NEC
	K63.3	Angiocardiography 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	Saphenous vein graft replacement of coronary artery
	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	K49	Transluminal balloon angioplasty of coronary artery
procedures and stents	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
	K50.2	, , , , ,
	K30.3	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 int
		coronary artery NEC
	K75.8	Other specified percutaneous transluminal balloon angioplasty and insertion of ster
		into coronary artery
	K75.9	Unspecified percutaneous transluminal balloon angioplasty and insertion of stent
	10.5	into coronary artery
mplantation of cardiac	K59	Cardioverter defibrillator introduced through the vein
	K59.1	Implantation of cardioverter defibrillator using one electrode lead
acemakers/defibrillators		
	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

K60Cardiac pacemaker system introduced through veinK60.1Implantation of intravenous cardiac pacemaker system NECK60.2Resiting of lead of intravenous cardiac pacemaker systemK60.3Renewal of intravenous cardiac pacemaker system NECK60.4Removal of intravenous cardiac pacemaker systemK60.5Implantation of intravenous aingle chamber cardiac pacemaker systemK60.6Implantation of intravenous dual chamber cardiac pacemaker systemK60.7Implantation of intravenous biventricular cardiac pacemaker systemK60.8Other specified cardiac pacemaker system introduced through veinK61.9Unspecified cardiac pacemaker system NECK61.1Implantation of cardiac pacemaker system NECK61.2Resiting of lead of cardiac pacemaker system NECK61.3Renewal of cardiac pacemaker system NECK61.4Removal of cardiac pacemaker system NECK61.5Implantation of single chamber cardiac pacemaker systemK61.6Implantation of dual chamber cardiac pacemaker systemK61.6Implantation of biventricular cardiac pacemaker systemK61.6Implantation of biventricular cardiac pacemaker systemK61.8Other specified other cardiac pacemaker systemK61.9Unspecified other cardiac pacemaker systemK61.9Unspecified other cardiac pacemaker systemK61.9Implantation of biventricular cardiac pacemaker systemK61.6Implantation of biventricular cardiac pacemaker systemK61.9Unspecified other cardiac pacemaker systemK61.9Unspecified other cardia	
<ul> <li>K60.2 Resiting of lead of intravenous cardiac pacemaker system</li> <li>K60.3 Renewal of intravenous cardiac pacemaker system NEC</li> <li>K60.4 Removal of intravenous cardiac pacemaker system</li> <li>K60.5 Implantation of intravenous single chamber cardiac pacemaker system</li> <li>K60.6 Implantation of intravenous dual chamber cardiac pacemaker system</li> <li>K60.7 Implantation of intravenous biventricular cardiac pacemaker system</li> <li>K60.8 Other specified cardiac pacemaker system introduced through vein</li> <li>K60.9 Unspecified cardiac pacemaker system introduced through vein</li> <li>K61.1 Implantation of cardiac pacemaker system NEC</li> <li>K61.2 Resiting of lead of cardiac pacemaker system NEC</li> <li>K61.3 Renewal of cardiac pacemaker system NEC</li> <li>K61.4 Removal of cardiac pacemaker system NEC</li> <li>K61.5 Implantation of single chamber cardiac pacemaker system</li> <li>K61.6 Implantation of biventricular cardiac pacemaker system</li> <li>K61.6 Implantation of biventricular cardiac pacemaker system</li> <li>K61.7 Implantation of biventricular cardiac pacemaker system</li> <li>K61.8 Other specified other cardiac pacemaker system</li> <li>K61.9 Unspecified other cardiac pacemaker system</li> <li>K61.9 Unspecified other cardiac pacemaker system</li> <li>K61.9 Unspecified other cardiac pacemaker system</li> <li>K61.9 Conservation of biventricular cardiac pacemaker system</li> <li>K61.9 Conservation of biventricular cardiac pacemaker system</li> <li>K61.9 Unspecified other cardiac pacemaker system</li> <li>K73 Other cardiac pacemaker system introduced through vein</li> <li>K73.1 Renewal of intravenous single chamber cardiac pacemaker system</li> <li>K73.2 Renewal of intravenous biventricular cardiac pacemaker system</li> <li>K73.3 Renewal of intravenous biventricular cardiac pacemaker system</li> </ul>	
<ul> <li>K60.3 Renewal of intravenous cardiac pacemaker system NEC</li> <li>K60.4 Removal of intravenous cardiac pacemaker system</li> <li>K60.5 Implantation of intravenous single chamber cardiac pacemaker system</li> <li>K60.6 Implantation of intravenous dual chamber cardiac pacemaker system</li> <li>K60.7 Implantation of intravenous biventricular cardiac pacemaker system</li> <li>K60.8 Other specified cardiac pacemaker system introduced through vein</li> <li>K60.9 Unspecified cardiac pacemaker system introduced through vein</li> <li>K61.0 Other cardiac pacemaker system</li> <li>K61.1 Implantation of cardiac pacemaker system NEC</li> <li>K61.2 Resiting of lead of cardiac pacemaker system NEC</li> <li>K61.3 Renewal of cardiac pacemaker system NEC</li> <li>K61.4 Removal of cardiac pacemaker system NEC</li> <li>K61.5 Implantation of single chamber cardiac pacemaker system</li> <li>K61.6 Implantation of biventricular cardiac pacemaker system</li> <li>K61.7 Implantation of biventricular cardiac pacemaker system</li> <li>K61.8 Other specified other cardiac pacemaker system NEC</li> <li>K61.4 Removal of cardiac pacemaker system NEC</li> <li>K61.5 Implantation of biventricular cardiac pacemaker system</li> <li>K61.8 Other specified other cardiac pacemaker system</li> <li>K61.9 Unspecified other cardiac pacemaker system</li> <li>K61.8 Other specified other cardiac pacemaker system</li> <li>K61.9 Unspecified other cardiac pacemaker system</li> <li>K73 Other cardiac pacemaker system introduced through vein</li> <li>K73.1 Renewal of intravenous single chamber cardiac pacemaker system</li> <li>K73.2 Renewal of intravenous biventricular cardiac pacemaker system</li> <li>K73.3 Renewal of intravenous biventricular cardiac pacemaker</li> </ul>	
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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 G42* Other fibreoptic endoscopic extirpation of lesion of upper gastrointestinal tract	
procedures (gastric, G42.1* Fibreoptic endoscopic submucosal resection of lesion of upper gastrointestina	tract
iejunum, ileum) G42.2* Fibreoptic endoscopic photodynamic therapy of lesion of upper gastrointestina	
G42.3* Fibreoptic endoscopic mucosal resection of lesion of upper gastrointestinal tra	
G42.8* Other specified other fibreoptic endoscopic extirpation of lesion of upper gastrointestinal tract	
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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	
G43.7* Fibreoptic endoscopic rubber band ligation of upper gastrointestinal tract	

	643.8*	Other specified fibreoptic endoscopic extirpation of lesion of upper gastrointestinal
		tract
	643.9* 644*	Unspecified fibreoptic endoscopic extirpation of lesion of upper gastrointestinal tract Other therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract
	644.1*	Fibreoptic endoscopic insertion of prosthesis into upper gastrointestinal tract
	644.2#	Fibreoptic endoscopic removal of foreign body from upper gastrointestinal tract
	644.3*	Fibreoptic endoscopic dilation of upper gastrointestinal tract NEC
	644.4#	Fibreoptic endoscopic reduction of intussusception of gastroenterostomy
	644.5*	Fibreoptic endoscopic percutaneous insertion of gastrostomy
	644.6*	Fibreoptic endoscopic pressure controlled balloon dilation of lower oesophageal
		sphincter
	644.7#	Fibreoptic endoscopic removal of gastrostomy tube
G	644.8*	Other specified other therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract
G	644.9*	Unspecified other therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract
G	645 <sup>#</sup>	Diagnostic fibreoptic endoscopic examination of upper gastrointestinal tract
	645.1*	Fibreoptic endoscopic examination of upper gastrointestinal tract and biopsy of
		lesion of upper gastrointestinal tract
	645.2#	Fibreoptic endoscopic ultrasound examination of upper gastrointestinal tract
	645.3#	Fibreoptic endoscopic insertion of Bravo pH capsule into upper gastrointestinal tract
G	645.4#	Fibreoptic endoscopic examination of upper gastrointestinal tract and staining of gastric mucosa
G	645.8#	Other specified diagnostic fibreoptic endoscopic examination of upper gastrointestinal tract
G	645.9#	Unspecified diagnostic fibreoptic endoscopic examination of upper gastrointestinal
		tract
	646*	Therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract
	646.1*	Fibreoptic endoscopic endoluminal plication of gastro-oesophageal junction
	646.2*	Fibreoptic endoscopic coagulation of bleeding lesion of upper gastrointestinal tract
G	646.8*	Other specified therapeutic fibreoptic endoscopic operations on upper gastrointestinal tract
	646.9*	Unspecified therapeutic fibreoptic endoscopic operations on upper gastrointestinal
		tract
	654*	Therapeutic endoscopic operations on duodenum
	654.1*	Endoscopic extirpation of lesion of duodenum
	654.2*	Endoscopic dilation of duodenum
	654.3*	Endoscopic insertion of tubal prosthesis into duodenum
	54.8*	Other specified therapeutic endoscopic operations on duodenum
	654.9*	Unspecified therapeutic endoscopic operations on duodenum
	655 <sup>#</sup>	Diagnostic endoscopic examination of duodenum
	655.1*	Diagnostic endoscopic examination of duodenum and biopsy of lesion of duodenum
	655.8 <sup>#</sup>	Other specified diagnostic endoscopic examination of duodenum
	655.9 <sup>#</sup>	Unspecified diagnostic endoscopic examination of duodenum
	64* 64.1*	Therapeutic endoscopic operations on jejunum
	64.1° 64.2*	Endoscopic extirpation of lesion of jejunum Endoscopic dilation of jejunum
	64.2* 64.3*	Endoscopic dilation of jejunum Endoscopic insertion of tubal prosthesis into jejunum
	64.8*	Other specified therapeutic endoscopic operations on jejunum
	64.9*	Unspecified therapeutic endoscopic operations on jejunum
	65 <sup>#</sup>	Diagnostic endoscopic examination of jejunum
	65.1*	Diagnostic endoscopic examination of jejunum and biopsy of lesion of jejunum
	65.8 <sup>#</sup>	Other specified diagnostic endoscopic examination of jejunum
	65.9 <sup>#</sup>	Unspecified diagnostic endoscopic examination of jejunum
	679*	Therapeutic endoscopic operations on ileum
	679.1*	Endoscopic extirpation of lesion of ileum
	679.2*	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 <sup>#</sup>	Wireless capsule endoscopy
	G80.3 <sup>#</sup>	Diagnostic endoscopic balloon examination of ileum
		Other specified diagnostic endoscopic examination of ileum
	G80.8 <sup>#</sup>	
	G80.9 <sup>#</sup>	Unspecified diagnostic examination of ileum
Lower GI endoscopic	H20*	Endoscopic extirpation of lesion of colon
procedures (including	H20.1*	Fibreoptic endoscopic snare resection of lesion of colon
sigmoid and rectum)	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 <sup>#</sup>	Fibreoptic endoscopic removal of foreign body from colon
	H21.4*	Fibreoptic endoscopic insertion of expanding metal stent into colon
	H21.5 <sup>#</sup>	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 <sup>#</sup>	Other specified diagnostic endoscopic examination of colon
	H22.9 <sup>#</sup>	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 <sup>#</sup>	Endoscopic decompression of lower bowel using fibreoptic sigmoidoscope
	H24.8*	Other specified other therapeutic endoscopic operations on lower bowel using fibreoptic sigmoidoscope

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	H24.9*	Unspecified other therapeutic endoscopic operations on lower bowel using fibreoptic sigmoidoscope
	H25#	Diagnostic endoscopic examination of lower bowel using fibreoptic sigmoidoscope
	H25.1*	Diagnostic endoscopic examination of lower bowel using interoptic signotoscope
	HZ3.1	bowel using fibreoptic sigmoidoscope
	H25.2 <sup>#</sup>	Diagnostic endoscopic examination of lower bowel and sampling for bacterial
	1105.0#	overgrowth using fibreoptic sigmoidoscope
	H25.8 <sup>#</sup>	Other specified diagnostic endoscopic examination of lower bowel using fibreoptic sigmoidoscope
	H25.9 <sup>#</sup>	Unspecified diagnostic endoscopic examination of lower bowel using fibreoptic 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
	H27.1 <sup>#</sup>	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 rigi sigmoidoscope
	H27.9*	Unspecified other therapeutic endoscopic operations on sigmoid colon using rigid sigmoidoscope
	H28 <sup>#</sup>	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 <sup>#</sup>	Other specified diagnostic endoscopic examination of sigmoid colon using rigid
	H28.9 <sup>#</sup>	sigmoidoscope Unspecified diagnostic endoscopic examination of sigmoid colon using rigid
<b>.</b>		sigmoidoscope
Colonic surgery (incl.	H01	Emergency excision of appendix
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 appendicectomy
	H02.2	Planned delayed appendicectomy NEC
	H02.3	Prophylactic appendicectomy NEC
	H02.4	Incidental appendicectomy
	H02.8	Other specified other excision of appendix
	H02.9	Unspecified other excision of appendix
	H03	Other operations on appendix

1100.4	
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 neosionly in Q
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
	2
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 of color to rectain
H10.3	Sigmoid colectomy and ileostomy HFQ
H10.4	
	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
	1120.1	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
	1120.0	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	J40	Endoscopic retrograde placement of prosthesis in bile duct
Cholangio-pancreatic	J40.1	Endoscopic retrograde insertion of tubal prostnesis into both hepatic ducts
	J40.1	Endoscopic retrograde insertion of tubal prosthesis into both hepatic ducts
Procedures (ERCP)	J40.2	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 prostnesis in bile duct
	J40.5 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
	J41.2	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
	J42.1	Endoscopic retrograde renewal of tubal prosthesis in pancreatic duct
	J42.2 J42.3	Endoscopic retrograde removal of calculus from pancreatic duct
	J42.3	Endoscopic retrograde drainage of lesion of pancreas
	J42.4 J42.5	Endoscopic retrograde dilation of pancreatic duct
	J42.5 J42.8	Other specified therapeutic endoscopic retrograde operations on pancreatic duct
	J42.0 J42.9	Unspecified therapeutic endoscopic retrograde operations on pancreatic duct
		Diagnostic endoscopic retrograde examination of bile duct and pancreatic duct
	J43 J43.1	Endoscopic retrograde cholangiopancreatography and biopsy of lesion of ampulla of
	J4J. I	Vater
	J43.2	
	J4J.Z	Endoscopic retrograde cholangiopancreatography and biopsy of lesion of biliary or
	J43.3	pancreatic system NEC
	J43.3 J43.8	Endoscopic retrograde cholangiopancreatography and collection of bile Other specified diagnostic endoscopic retrograde examination of bile duct and
	J <del>4</del> J.0	pancreatic duct
	1/3 0	
	J43.9	Unspecified diagnostic endoscopic retrograde examination of bile duct and
	J44	pancreatic duct Diagnostic andoscopic retrograde examination of hile duct
		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 J45	Unspecified diagnostic endoscopic retrograde examination of bile duct Diagnostic endoscopic retrograde examination of pancreatic duct
	J45 J45.1	
		Endoscopic retrograde pancreatography and biopsy of lesion of pancreas
	J45.2 J45.3	Endoscopic retrograde pancreatography and collection of pancreatic juice
		Endoscopic retrograde pancreatography through accessory ampulla of Vater
	J45.8 J45.9	Other specified diagnostic endoscopic retrograde examination of pancreatic duct
	J45.9	Unspecified diagnostic endoscopic retrograde examination of pancreatic duct
GU 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

	M30	Diagnostic endoscopic examination of ureter
	M30.1	Endoscopic retrograde pyelography
	M30.2	Endoscopic catheterisation of ureter
	M30.2	Endoscopic ureteric urine sampling
	M30.4	Nephroscopic ureteroscopy
	M30.4	
		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
	M43.4	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
	M44.1	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	M65	Endoscopic resection of outlet of male bladder
procedures	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
	101.2	

V167.3 V167.4	Endoscopic drainage of prostate Endoscopic removal of calculus from prostate
	Endoscopic removal of calculus from prostate
M67.5	Endoscopic microwave destruction of lesion of prostate
	Endoscopic radiofrequency ablation of lesion of prostate
	Other specified other therapeutic endoscopic operations on prostate
	Unspecified other therapeutic endoscopic operations on prostate
	Endoscopic insertion of prosthesis into prostate
	Endoscopic insertion of prostatic stent
	Endoscopic removal of prostatic stent
M68.3	Endoscopic insertion of prosthesis to compress lobe of prostate
	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
	Other specified other operations on prostate
	Unspecified other operations on prostate
-48	Therapeutic fibreoptic endoscopic operations on lower respiratory tract
	Fibreoptic endoscopic snare resection of lesion of lower respiratory tract
	Fibreoptic endoscopic laser destruction of lesion of lower respiratory tract
	Fibreoptic endoscopic destruction of lesion of lower respiratory tract NEC
	Fibreoptic endoscopic aspiration of lower respiratory tract
	Fibreoptic endoscopic removal of foreign body from lower respiratory tract
	Fibreoptic endoscopic irrigation of lower respiratory tract
	Fibreoptic endoscopic photodynamic therapy of lesion of lower respiratory tract
	Other specified therapeutic fibreoptic endoscopic operations on lower respiratory
_+0.0	tract
E48.9	Unspecified therapeutic fibreoptic endoscopic operations on lower respiratory tract
E49	Diagnostic fibreoptic endoscopic examination of lower respiratory tract
E49.1	Diagnostic fibreoptic endoscopic examination of lower respiratory tract and biopsy of
	lesion of lower respiratory tract
E49.2	Diagnostic fibreoptic endoscopic examination of lower respiratory tract and lavage of
- 40.0	lesion of lower respiratory tract
=49.3	Diagnostic fibreoptic endoscopic examination of lower respiratory tract and brush cytology of lesion of lower respiratory tract
E49.4	Diagnostic fibreoptic endoscopic examination of lower respiratory tract with lavage and brush cytology of lesion of lower respiratory tract
E49.5	Diagnostic fibreoptic endoscopic examination of lower respiratory tract with biopsy,
	lavage and brush cytology of lesion of lower respiratory tract
-49.8	Other specified diagnostic fibreoptic endoscopic examination of lower respiratory tract
E49.9	Unspecified diagnostic fibreoptic endoscopic examination of lower respiratory tract
E50	Therapeutic endoscopic operations on lower respiratory tract using rigid bronchoscope
=50.1	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
	168.8       168.9         168.8       168.9         170.1       170.1         170.2       170.3         170.3       170.4         170.5       170.6         170.7       170.8         170.9       171         171.1       171.2         171.8       171.9         48       48.1         48.48.1       48.2         448.3       448.5         448.4       48.5         448.8       448.7         448.8       448.7         448.9       449.1         449.1       449.2         449.3       449.3         449.4       449.5         50       50         50       50

	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 &	E20	Operations on adenoid
Adenoidectomy	E20.1	Total adenoidectomy
rachelacotomy	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	E06	Packing of cavity of nose
intubation	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		
Procedures	X32	Exchange blood transfusion
	X32 X32.1	Exchange blood transfusion Neonatal exchange blood transfusion

X2.2       Exchange of plasma (1-9)         X2.3       Exchange of plasma (1-9)         X2.4       Exchange of plasma (1-9)         X2.5       Exchange of plasma (1-9)         X2.4       Eucopheresis         X2.2       Unpercified exchange blood transfusion         X3.3       Untre-arterial blood transfusion         X3.3       Intra-arterial blood transfusion of packed cells         X3.3       Intra-arterial blood transfusion of platelets         X3.3       Intra-arterial blood transfusion         X3.4       Autologous peripheral blood stem cell transplant         X3.3       Styperice peripheral blood transfusion         X3.3       Unspecified other blood transfusion         X3.3       Unspecified other blood transfusion         X3.4       Autologous transfusion of transfusion         X3.3       Unspecified other blood transfusion         X3.4       Autologous transfusion of factor         X4.4       Transfusion of factor         X4.4       Transfusion of transfusion         X4.4       Transfusion of toke spender         X4.3       Transfusion of toke spender         X4.3       Totastistion af curve transfusion         X4.4       Unspecified other intravenous transfusion         X4.5		X32.3	Exchange of plasma $(2,0)$
X2.5       Exchange of pissma (>19)         X2.6       Red cell servicing         X2.7       Leucopheresis         X2.8       Other specified exchange blood transfusion         X2.8       Unspecified exchange blood transfusion         X3.1       Intra-enterial blood transfusion of packed cells         X3.3       Intra-enterial blood transfusion         X3.3       Intra-enterial blood transfusion         X3.4       Autologous transfusion of packed cells         X3.3       Intra-enterial blood transfusion         X3.3       Other specified other blood transfusion         X3.4       Unspecified other intravenous transfusion         X3.4       Transfusion of blood expander         X3.4       Transfusion of blood expander         X3.4       Transfusion of cave unterase of uterus         Procedures       Other specified other intravenous transfusion         X3.4       Transfusion of cave unterase of uterus NEC         Obstetric & gynae       Procedures         Proc			Exchange of plasma (2-9)
X22.6       Red cell exchange         X23.0       Other specified exchange blood transfusion         X23.0       Unspecified exchange blood transfusion         X33.1       Intra-arterial blood transfusion         X33.1       Intra-arterial blood transfusion of packed cells         X33.3       Intra-arterial blood transfusion of packed cells         X33.3       Intra-arterial blood transfusion of packed cells         X33.3       Intra-arterial blood stem cell transplant         X33.5       Syngeneic peripheral blood stem cell transplant         X33.5       Syngeneic peripheral blood stem cell transplant         X33.7       Autologous transfusion of action         X34.3       Unspecified other blood transfusion         X34.3       Unspecified other blood transfusion         X34.3       Unspecified other intravenous transfusion         X			
X327         Leucopheresis           X328         Other specified exchange blood transfusion           X33         Other specified exchange blood transfusion           X33         Other blood transfusion           X33         Other blood transfusion           X33         Intra-venous blood transfusion of packed cells           X333         Intra-venous blood transfusion of packed cells           X333         Intra-venous blood transfusion of packed cells           X334         Autologous peripheral blood stem cell transplant           X335         Syngeneic peripheral blood transfusion           X337         Autologous transfusion of red blood cells           X338         Other specified dreft intravenous transfusion           X341         Transfusion of coegulation factor           X342         Transfusion of blood expander           X343         Other precedited other intravenous transfusion           X343         Other precedited other intravenous transfusion           X348         Other specified dreft intravenous transfusion           X344         Other precedited other intravenous transfusion           X343         Other specified dreft intravenous transfusion           X344         Other specified dreft intravenous transfusion           X345         Other specified dreft rege of uterus<			
X32.8       Other specified exchange blood transfusion         X33       Other blood transfusion         X33       Other blood transfusion         X33       Intraveneral blood transfusion of packed cells         X33.1       Intravenous blood transfusion of packed cells         X33.2       Intravenous blood transfusion of packed cells         X33.3       Intravenous blood transfusion of packed cells         X33.4       Autologous perioperal blood stem cell transplant         X35.5       Syngencic peripheral blood stem cell transplant         X37.7       Autologous transfusion         X38.8       Other specified duter blood transfusion         X34.1       Transfusion of pasma NEC         X34.2       Transfusion of blood sepander         X34.3       Other specified duter blood sepander         X34.8       Other specified duter blood sepander         X34.9       Unspecified duter intravenous transfusion         X34.0       Other specified duter intrav			
X32.9         Unspecified exchange blood transfusion           X33         Other blood transfusion           X33         Intra-enterial blood transfusion of packed cells           X33.1         Intravenous blood transfusion of packed sells           X33.2         Intravenous blood transfusion of packed sells           X33.4         Autologous peripheral blood stem cell transplant           X33.6         Allogeneic peripheral blood transfusion           X33.8         Other specified other blood transfusion           X34.4         Other intravenous transfusion           X34.3         Other intravenous transfusion           X34.4         Other intravenous transfusion           X34.3         Transfusion of secum NEC           X34.3         Other intravenous transfusion           X34.3         Other intravenous transfusion           X34.3         Other intravenous transfusion           X34.3         Other intravenous transfusion           X34.3         Other specified other intravenous transfusion           X34.3         Other specified other intravenous transfusion           X34.3         Other specified other intravenous transfusion           X34.4         Transfusion of blood expander           X34.5         Other specified other execusion           Obstetric & gynae <td></td> <td></td> <td></td>			
X33         Other blood transfusion           X33.1         Intra-antrail blood transfusion of packed cells           X33.2         Intravenous blood transfusion of packed cells           X33.3         Intravenous blood transfusion of patelets           X33.4         Autologous peripheral blood stem cell transplant           X35.5         Syngencic peripheral blood stem cell transplant           X33.6         Allogencic peripheral blood transfusion           X33.8         Other specified other blood transfusion           X33.9         Unspecified other blood transfusion           X33.9         Unspecified other blood transfusion           X34.3         Transfusion of coagulation factor           X34.4         Transfusion of blood segmader           X34.8         Other specified other blood segmader           X34.8         Other specified other intravenous transfusion           X34.8         Other specified other intravenous transfusion           X34.8         Other specified other intravenous transfusion           V34.9         Unspecified other intravenous transfusion           V36.7         Itarspecified other intravenous transfusion           X34.8         Other specified other intravenous transfusion           Costettric & gymae         Costettric & gymae           procedures         Q10 </td <td></td> <td></td> <td></td>			
X331       Intra-encus biod transfusion of patelets         X332       Intravenous biod transfusion of patelets         X334       Autologous peripheral blood stem cell transplant         X335       Syngenetic peripheral blood stem cell transplant         X336       Allogeneic peripheral blood stem cell transplant         X337       Autologous transfusion of red blood cells         X338       Other specified dret blood transfusion         X339       Unspecified other blood transfusion         X341       Transfusion of rea blood transfusion         X343       Other intravenous transfusion         X341       Transfusion of coagulation factor         X342       Transfusion of blood expander         X348       Other intravenous transfusion         X349       Unspecified other intravenous transfusion         X340       Corretage of ulerus         Coretage of ulerus       Coretage of roducts of con			
X332       Intravenous blood transfusion of patelets         X333       Hutorenous blood transfusion of patelets         X334       Autologous peripheral blood stem cell transplant         X335       Rilogous peripheral blood stem cell transplant         X337       Autologous transfusion of red blood cells         X338       Other specified other blood transfusion         X331       Other specified other blood transfusion         X332       Other specified other blood transfusion         X334       Other intravenous transfusion         X341       Transfusion of opaulation factor         X342       Transfusion of bloed expander         X343       Other specified other intravenous transfusion         Bone marrow puncture       W36.5         V66.7       Harvest of bone marrow         Verating of products of conception from uterus NEC         Y66.7       Harvest of bone marrow         Obstetric & gynae       Q101         Outcretage of products of conception from uterus NEC         Q102       Curetage of products of conception from uterus NEC         Q103       Ditation of cervix uteri and curetage of uterus         Q104       Curetage of products of conception from uterus NEC         Q103       Ditation of products of conception from uterus NEC			
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         X33.4       Other intravenous transfusion         X33.4       Other intravenous transfusion         X34.1       Transfusion of coagulation factor         X34.2       Transfusion of blood expander         X34.3       Transfusion of blood spender         X34.8       Other specified other intravenous transfusion         X34.9       Unspecified other intravenous transfusion         X34.9       Other vacation of bone marrow NEC         Porcedures       Vior         Q10       Curetlage of uterus         Curetlage of ruducts of conception from uterus NEC         Q10.1       Curetlage of products of conception from uterus NEC         Q11.0       Unspecified curettage of uterus			
X33.4         Autologous peripheral blood stem cell transplant           X33.5         Syngeneic peripheral blood stem cell transplant           X33.6         Altologous transfusion of red blood cells           X33.8         Other specified other blood transfusion           X33.9         Other specified other blood transfusion           X33.9         Other specified other blood transfusion           X33.4         Other specified other blood transfusion           X34.1         Transfusion of caputation factor           X34.2         Transfusion of serum NEC           X34.3         Transfusion of serum NEC           X34.4         Transfusion of blood expander           X34.9         Unspecified other intravenous transfusion           Bone marrow puncture         W36.5         Diagnostic extraction of bone marrow NEC           Y66.7         Harvest of bone marrow         Y66.7           Abortion/dilitation &         Q10         Curetlage of uterus           curetlage         Q10.1         Dilation of cervix uteri and curetlage of uterus NEC           Q10.8         Curetlage of orducts of conception from uterus NEC           Q10.9         Unspecified other revacuation of products of conception from uterus NEC           Q10.8         Dilation of cervix uteri and curetlage of uterus           Q11.0			
X33.5       Syngenic peripheral blood stem cell transplant         X33.6       Allogenic peripheral blood tem cell transplant         X33.7       Autologous transfusion of red blood cells         X33.8       Other specified other blood transfusion         X34.0       Other intravenous transfusion         X34.1       Transfusion of coegulation factor         X34.2       Transfusion of serum NEC         X34.3       Unspecified other blood transfusion         X34.3       Transfusion of serum NEC         X34.3       Unspecified other intravenous transfusion         X34.4       Transfusion of bloom expander         X34.5       Unspecified other intravenous transfusion         W35.5       Diagnostic extraction of bone marrow NEC         Y66.7       Harvest of bone marrow         Obstetric & gynae       Q10         Curetlage of urdusts of conception from uterus       NEC         Q10.1       Curetlage of orducts of conception from uterus         Q10.2       Curetlage of uterus         Q10.3       Unspecified outer steage of uterus         Q11.4       Other execuation of products of conception from uterus NEC         Q12.5       Unspecified outer execuation of products of conception from uterus NEC         Q11.4       Other specified outere vacuation of produc			
X33.6       Allogeneic peripheral blood stem cell transplant         X33.7       Autologous transitusion of red blood cells         X33.8       Other specified other blood transitusion         X34       Other intravenous transitusion         X34       Other intravenous transitusion         X34.1       Transitusion of coegulation factor         X34.2       Transitusion of plasma NEC         X34.3       Transitusion of plasma NEC         X34.4       Transitusion of blood expander         X34.9       Other specified other intravenous transitusion         X34.9       Unspecified other intravenous transitusion         X34.9       Other specified other intravenous transitusion         X34.9       Unspecified other intravenous transitusion         V349       Unspecified other intravenous transitusion         Valgonal transitusion of envix uteri and curetage of products of conception from uterus         Obstetric & gynae       Procedures         Procedures       Q10       Curetage of uterus         Q11.0       Dilation of cervix uteri and curetage of products of conception from uterus			
X33.7       Autologous transfusion of red blood cells         X33.9       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 serum NEC         X34.3       Transfusion of serum NEC         X34.3       Transfusion of blood expander         X34.3       Unspecified other intravenous transfusion         W35.5       Diagnostic extraction of bone marrow NEC         V66.7       Harvest of bone marrow         Procedures       Q10         Abortion/dilation 8       Q10         Curetlage of uterus       Q10.1         Dilation of cervix uteri and curetlage of products of conception from uterus         Q10.1       Dilation of cervix uteri and curetlage of uterus NEC         Q10.2       Curetlage of uterus         Q11.1       Dilation of conception from uterus NEC         Q13.2       Dilation of products of conception from uterus NEC         Q13.3       Evacuation of products of conception from uterus NEC         Q11.4       Other specified other evacuation of contents of uterus         Q11.1       Vacuum aspiration of products of conception from uterus NEC         Q11.3			
X33.8       Other specified other blood transfusion         X33.9       Unspecified other blood transfusion         X34       Other intravenous transfusion         X34.1       Transfusion of cogulation factor         X34.2       Transfusion of plasma NEC         X34.3       Transfusion of blood expander         X34.4       Transfusion of blood expander         X34.8       Other specified other intravenous transfusion         X34.9       Unspecified other intravenous transfusion         W35.5       Diagnostic extraction of bone marrow NEC         Y66.7       Harvest of bone marrow         Obstetric & gynae       Procedures         Abortion/dilatation &       O10         Curetage of uterus       Curetage of uterus         curetage       O11.1         Dilation of cervix uteri and curetage of troucus of conception from uterus         Q10.2       Curetage of uterus         Q11.3       Dilation of products of conception from uterus NEC         Q10.4       Other specified curetage of uterus         Q11.1       Vacuum aspiration of products of conception from uterus NEC         Q11.2       Dilation of cervix uteri and evacuation of conducts of conception from uterus NEC         Q11.4       Extraction of menses         Q11.1       Vac			
X33.9       Unspecified other blood transfusion         X34       Other intravenous transfusion         X34.1       Transfusion of cacquilation factor         X34.3       Transfusion of sequent factor         X34.4       Transfusion of blood expander         X34.4       Transfusion of blood expander         X34.4       Unspecified other intravenous transfusion         X34.4       Unspecified other intravenous transfusion         X34.9       Unspecified other intravenous transfusion         X34.9       Unspecified other intravenous transfusion         X34.9       Unspecified other intravenous transfusion         Obstetric & gynae       Y66.7         Procedures       Y101         Abortion/dilatation &       Q10         Curettage of ulerus       Q10.2         Q10.1       Dilation of cervix uteri and curettage of products of conception from uterus NEC         Q10.8       Other specified curettage of uterus         Q10.9       Unspecified curettage of uterus         Q11.1       Vacuum aspiration of products of conception from uterus NEC         Q11.1       Vacuum aspiration of products of conception from uterus NEC         Q11.1       Vacuum aspiration of products of conception from uterus using fiexible cannula         Q11.1       Vacuum aspiration of pro			
X34         Other intravenous transfusion           X34.1         Transfusion of cagulation factor           X34.2         Transfusion of Jasma NEC           X34.3         Transfusion of blasma NEC           X34.4         Transfusion of blood expander           X34.8         Other specified other intravenous transfusion           X34.9         Unspecified other intravenous transfusion           X34.7         Transfusion of products of conception from uterus frection           Obstetric & gynae         Proceedures           Abortion/dilatation &         Q10         Curettage of uterus           Q10.1         Dilation of cervix uteri and curettage of uterus NEC           Q10.2         Curettage of uterus         Q11.1           Q10.2         Curettage of uterus         Q11.1           Q11.2         Dilation of cervix uteri and exacuation of products of conception from uterus NEC			
X34.1       Transfusion of coagulation factor         X34.2       Transfusion of plasma NEC         X34.3       Transfusion of blood expander         X34.4       Transfusion of blood expander         X34.8       Other specified other intravenous transfusion         X34.9       Unspecified other intravenous transfusion         Obstetric & gynae       Procedures         Abortion/dilatation &       Q10       Curettage of uterus         Autoritian       Q10.1       Dilation of cervix uteri and curettage of products of conception from uterus         Q10.2       Curettage of uterus       Q10.2         Q10.3       Dilation of cervix uteri and curettage of uterus NEC         Q10.4       Q10.5       Q10.9         Q10.9       Unspecified curettage of uterus         Q11.0       Other evacuation of products of conception from uterus NEC         Q11.2       Dilation of products of conception from uterus NEC         Q11.3       Evacuation of products of conception from uterus NEC         Q11.4       Extraction delivery         Q11.5       Vacuum aspiration of products of conception			
X34.2       Transfusion of plasma NEC         X34.3       Transfusion of blood expander         X34.4       Transfusion of blood expander         X34.3       Other specified other intravenous transfusion         X34.9       Unspecified other intravenous transfusion         W35.5       Diagnostic extraction of bone marrow NEC         Y66.7       Harvest of bone marrow         Obstetric & gynae procedures       Q10       Curettage of uterus         Abortion/dilatation & Curettage       Q10       Curettage of products of conception from uterus         Q10.2       Curettage of products of conception from uterus NEC       Q10.3         Q10.3       Dilation of cervix uteri and curettage of uterus       Q10.4         Q10.4       Urterspecified curettage of uterus       Q10.4         Q10.5       Urterspecified curettage of uterus       Q11.1         Q10.4       Urter evacuation of products of conception from uterus NEC       Q11.2         Q11.4       Extraction of menses       Q11.2       Dilation of cervix uteri and evacuation of products of uterus         Q11.1       Vacuum aspiration of products of conception from uterus using figid cannula       Q11.3       Evacution of products of conception from uterus using figid cannula         Q11.4       Extraction delivery       R19       Breech extraction delivery			
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       W35.5       Diagnostic extraction of bone marrow NEC         Y66.7       Harvest of bone marrow       Y66.7         Obstetric & gynae procedures       Q10       Currettage of uterus         Abortion/vilitation & currettage       Q10.1       Curettage of products of conception from uterus NEC         Q10.2       Curettage of products of conception from uterus NEC       Q10.8         Q10.3       Dilation of cervix uteri and curettage of uterus       Q10.1         Q11.0       Other specified curettage of uterus       Q11.1         Q11.0       Unspecified curettage of uterus       Q11.1         Q11.1       Vacuum aspiration of products of conception from uterus NEC       Q11.2         Q11.4       Extraction or menses       Q11.5       Vacuum aspiration of products of conception from uterus NEC         Q11.5       Vacuum aspiration of products of conception from uterus using figid cannula       Q11.6       Vacuum aspiration of products of conception from uterus         Q11.5       Other specified other evacuation of contents of uterus       Q11.9       Q11.9       Q11.9			
X34.4       Transfusion of blood expander         X34.8       Other specified other intravenous transfusion         X34.9       Unspecified other intravenous transfusion         X34.9       Unspecified other intravenous transfusion         Bone marrow puncture       W36.5       Diagnostic extraction of bone marrow NEC         Obstetric & gynae       Y66.7       Harvest of bone marrow         Procedures       Abortion/dilatation &       O10       Curettage of uterus         Abortion/dilatation &       O11       Dilation of cervix uteri and curettage of products of conception from uterus NEC         Q10.3       Dilation of cervix uteri and curettage of uterus       Q10.0         Q11.0       Diter evacuation of conception from uterus NEC         Q10.3       Unspecified curettage of uterus         Q11.1       Dilation of cervix uteri and curettage of uterus         Q10.3       Unspecified curettage of uterus         Q11.4       Other evacuation of conception from uterus NEC         Q11.1       Vacuum aspiration of products of conception from uterus NEC         Q11.1       Vacuum aspiration of products of conception from uterus NEC         Q11.4       Extraction of menses         Q11.5       Vacuum aspiration of products of conception from uterus using field cannula         Q11.6       Other specified othe			
X34.8       Other specified other intravenous transfusion         X34.9       Unspecified other intravenous transfusion         Bone marrow puncture       W36.5         Dispositic extraction of bone marrow NEC         Y66.7       Harvest of bone marrow         Obstetric & gynae procedures       Q10         Abortion/dilatation & curettage       Q10.1         Q10.1       Dilation of cervix uteri and curettage of products of conception from uterus Q10.2         Q10.3       Dilation of cervix uteri and curettage of uterus NEC         Q10.3       Dilation of contrix ideri and curettage of uterus NEC         Q10.9       Unspecified curettage of uterus         Q11.1       Vacuum aspiration of orolucts of conception from uterus NEC         Q11.2       Dilation of cervix uteri and evacuation of products of conception from uterus NEC         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         Q11.1       Vacuum aspiration of products of conception from uterus NEC         Q11.2       Dilation of products of conception from uterus NEC         Q11.4       Extraction of envix uteri and evacuation of contents of uterus         Q11.5       Vacuum aspiration of products of conception from uterus NEC         Q11.4 <t< td=""><td></td><td></td><td></td></t<>			
X34.9       Unspecified other intravenous transfusion         Bone marrow puncture       Y36.5       Diagnostic extraction of bone marrow NEC         Y66.7       Harvest of bone marrow         Obstetric & gynae procedures       Q10       Curettage of uterus         Abortion/dilatation & curettage       Q10       Curettage of products of conception from uterus NEC         Q10.3       Dilation of cervix uteri and curettage of products of conception from uterus Q10.2       Curettage of uterus         Q10.4       Curettage of products of conception from uterus NEC       Q10.3         Q10.3       Dilation of cervix uteri and curettage of uterus       Q10.4         Q10.4       Other specified curettage of uterus       Q10.4         Q11.1       Other evacuation of products of conception from uterus NEC       Q11.4         Q11.1       Vacuum aspiration of products of conception from uterus NEC       Q11.4         Q11.1       Vacuum aspiration of products of conception from uterus using rigid cannula         Q11.4       Extraction delivery       Q11.9         Q11.9       Unspecified other evacuation of contents of uterus         Q11.1       Usacuim aspiration of products of conception from uterus using rigid cannula         Q11.5       Vacuum aspiration of products of conception from uterus using rigid cannula         Q11.6       Vacuum aspira			
Bone marrow puncture         W36.5         Diagnostic extraction of bone marrow NEC           Y66.7         Harvest of bone marrow           Obstetric & gynae         Procedures           Abortion/dilatation & curettage of uterus         Q10         Curettage of uterus and curettage of products of conception from uterus Q10.2           Q10.1         Dilation of cervix uteri and curettage of uterus NEC         Q10.3         Dilation of cervix uteri and curettage of uterus NEC           Q10.9         Unspecified curettage of uterus         Q11.0         Unspecified curettage of uterus           Q11.1         Vacuum aspiration of products of conception from uterus NEC         Q11.3         Q11.1           Q11.1         Vacuum aspiration of products of conception from uterus NEC         Q11.3         Evacuation of products of conception from uterus NEC           Q11.1         Vacuum aspiration of products of conception from uterus NEC         Q11.4         Evacuation of products of conception from uterus NEC           Q11.2         Dilation of cervix uteri and evacuation of contents of uterus         Q11.4         Evacuation of products of conception from uterus NEC           Q11.1         Vacuum aspiration of products of conception from uterus sing rigid cannula         Q11.6         Vacuum aspiration of products of conception from uterus NEC           Q11.1         Vacuum aspiration of products of contents of uterus         Q11.9         Unspeci			
Y66.7         Harvest of bone marrow           Obstetric & gynae procedures         Curettage of uterus           Abortion/dilatation & curettage         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           Q10.3         Dilation of cervix uteri and curettage of uterus         Q10.4         Q10.9         Unspecified curettage of uterus           Q11.1         Other evacuation of contents of uterus         Q11.1         Q10.9         Unspecified curettage of uterus           Q11.1         Other evacuation of contents of conception from uterus NEC         Q11.2         Q11.1         Q10.1           Q11.1         Vacuum aspiration of products of conception from uterus NEC         Q11.3         Evacuation of products of conception from uterus NEC           Q11.2         Dilation of cervix uteri and evacuation of products of conception from uterus NEC         Q11.4         Extraction of products of conception from uterus NEC           Q11.4         Evacuation of products of conception from uterus using rigid cannula         Q11.6         Vacuum aspiration of products of conception from uterus using flexible cannula           Q11.9         Unspecified other evacuation of contents of uterus         Q11.9         Unspecified other vercentindelivery	Bone marrow puncture		
Obstetric & gynae procedures         Oliditiation &           Abortion/dilatation &         Curettage of uterus           Curettage         Olio         Curettage of products of conception from uterus NEC           Q10.2         Curettage of products of conception from uterus NEC           Q10.3         Dilation of cervix uteri and curettage of uterus           Q10.9         Unspecified curettage of uterus           Q11.1         Other specified curettage of uterus           Q11.2         Other specified curettage of uterus           Q11.3         Other specified curettage of uterus           Q11.1         Vacuum aspiration 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 NEC           Q11.4         Extraction of products of conception from uterus using rigid cannula           Q11.6         Vacuum aspiration of products of conception from uterus using rigid cannula           Q11.8         Other specified other evacuation of contents of uterus           Q11.9         Unspecified other evacuation of contents of uterus           Q11.9         Breech extraction delivery           Q11.9         Breech extraction delivery           Q11.9	Dono manow punctaro		
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           Q10.4         Other specified curettage of uterus           Q10.9         Unspecified curettage 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 products of conception from uterus NEC           Q11.4         Extraction of products of conception from uterus using rigid cannula           Q11.5         Vacuum aspiration of products of conception from uterus using rigid cannula           Q11.6         Vacuum aspiration of products of conception from uterus using rigid cannula           Q11.5         Vacuum aspiration of products of conception from uterus           Q11.9         Unspecified other evacuation of contents of uterus           Q11.9         Unspecified other evacuation of contents of uterus           Q11.9         Breech extraction delivery           R19 <td>Obstetric &amp; gynae</td> <td></td> <td></td>	Obstetric & gynae		
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	S42.4           S42.8           S42.9           S47           S47.1           S47.2           S47.3           S47.4           S47.5           S47.6           S47.8           S47.9           S54           S54.1	Resuture of skin NECOther specified suture of skin of other siteUnspecified suture of skin of other siteOpening of skinDrainage of lesion of skin of head or neckDrainage of lesion of skin NECIncision of lesion of skin NECIncision of lesion of skin NECIncision of skin of head or neckIncision of skin of head or neckIncision of skin NECIncision of skin of head or neckIncision of skin NECUnspecified opening of skinUnspecified opening of skinExploration of burnt skin of head or neckDebridement of burnt skin of head or neck

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	S54.5	Dressing of burnt skin of head or neck NEC Attention to dressing of burnt skin of head or neck
	S54.5 S54.6	
	S54.0 S54.7	Cleansing and sterilisation of burnt skin of head or neck
		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	F09	Surgical removal of tooth
removal of teeth	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
	F10.1	Upper dental clearance
	F10.2	Lower dental clearance
	F10.3	Extraction of multiple teeth NEC
	F10.4	Other specified simple extraction of tooth
	F10.0 F10.9	Unspecified simple extraction of tooth
Other oral ourginal	F10.9 F01	Partial excision of lip
Other oral surgical	F01 F01.1	Excision of vermilion border of lip and advancement of mucosa of lip
procedures	F01.1 F01.8	
		Other specified partial excision of lip
	F01.9	Unspecified partial excision of lip
	F02 F02.1	Extirpation of lesion of lip
	FUZ.1	Excision of lesion of lip

500.0	
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
F04.1	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
F22.1	Partial glossectomy
F22.2 F22.8	Other specified excision of tongue
F22.0	Unspecified excision of tongue
F22.9 F23	Extirpation of lesion of tongue
F23 F23.1	
F23.1 F23.2	Excision of lesion of tongue 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
F24.2	Glossotomy
F24.3	Other specified incision of tongue
F24.0	Unspecified incision of tongue
F24.9	Other operations on tongue
F26.1	Commissurectomy of tongue
F26.2	Excision of frenulum of tongue
F20.2 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
F20.9 F29	Correction of deformity of palate
F29 F29.1	Primary repair of cleft palate
F29.1 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
F30.1	Plastic repair of palate using flap of skin
F30.2	Plastic repair of palate using flap of tongue
F30.4	Plastic repair of palate using graft of skin
F30.4	Plastic repair of palate using grant of skin 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
F32.4	Uvulopalatopharyngoplasty
F32.5 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	Reonstruction 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	F16.4	Scaling of tooth
procedures		
	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	F13.1	Full restoration of crown of tooth
Procedures	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, <sup>#</sup> = 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 11month control period for 14,731 patients admitted with IE.

Invasive Procedures (IPs)	Case Period (4m)		Control Period (11m)		Unadjusted step model <sup>ь</sup>		Adjusted step-model <sup>c</sup>		
	Total proc <sup>a</sup>	Proc/m <sup>a</sup>	Total proc <sup>a</sup>	Proc/m <sup>a</sup>	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	7.54	100.0	007	00.0	2.45	2.20 10 2.09	1.45	1.20 10 1.09	0.007
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

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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) 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.

Heart

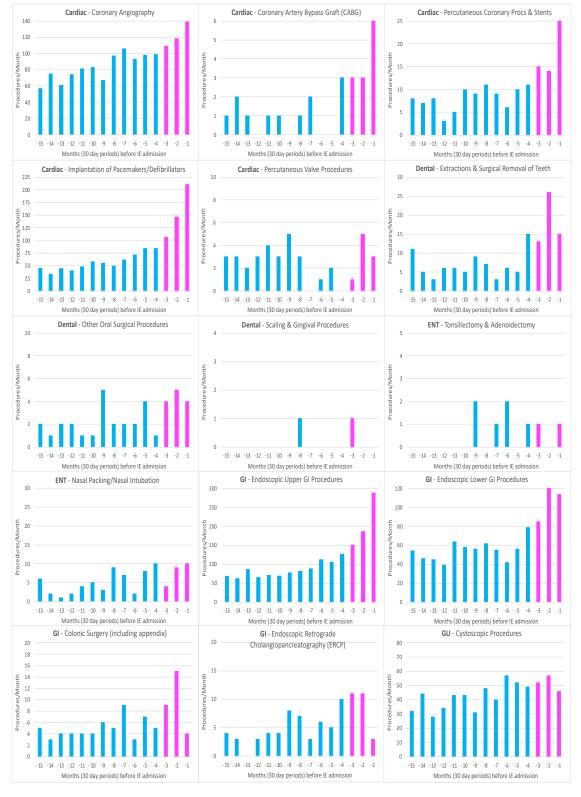
**Table S7.** Case-crossover step-analysis comparing the incidence of invasive procedures (IPs) using a 6-month case period and preceding 9-month control period for 14,731 patients admitted with IE.

Invasive Procedures (IPs)	Case Period (4m)		Control Period (11m)		Unadjusted step model <sup>b</sup>		Adjusted step-model <sup>c</sup>			
	Total proc <sup>a</sup>	Proc/m <sup>a</sup>	Total proc <sup>a</sup>	Proc/m <sup>a</sup>	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	069	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	

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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) 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.

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## 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.

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