Risk of infection following semi-invasive ultrasound procedures in Scotland, 2010 to 2016

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Full Title Risk of infection following semi-invasive ultrasound procedures in Scotland, 2010 to 2016: a retrospective cohort study using linked national datasets

Running Title Infection risk of ultrasound procedures

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Abstract

Introduction: Outbreak reports indicate a risk of cross-infection following medical procedures using semi-invasive ultrasound probes (SIUPs). This study aimed to evaluate the risk of infection, using microbiological reports and antibiotic prescriptions as proxy measures, associated with SIUP procedures, including transoesophageal echocardiography (TOE), transvaginal (TV) and transrectal (TR) ultrasound.

Methods: Patient records from the Electronic Communication of Surveillance in Scotland (ECOSS) and the Prescribing Information System (PIS) were linked with the Scottish Morbidity Records (SMR) for cases in Scotland between 2010 and 2016. Three retrospective cohorts were created to include inpatients/day-cases and outpatients in the following specialties: Cardiology, Gynaecology and Urology. Cox regression was used to quantify the association between SIUP procedures and the risk of positive microbiological reports and community antibiotic prescriptions in the 30-day period following the procedure.

Results: There was a greater hazard ratio (HR) of microbiological reports for patients who had undergone TOE (HR: 4.92; 95% CI: 3.17–7.63), TV (HR: 1.41; 95% CI: 1.21–1.64) and TR ultrasound (HR: 3.40; 95% CI: 2.90–3.99), compared with unexposed cohort members after adjustment for age, co-morbidities, previous hospital admissions and past care home residence. Similarly, there was a greater HR of antibiotic prescribing for those who had received TV (HR: 1.26; 95% CI: 1.20–1.32) and TR (HR: 1.75; 95% CI: 1.66–1.84) ultrasound, compared with unexposed patients.

Conclusion: Analysis of linked national datasets demonstrated a greater risk of infection within 30 days of undergoing SIUP procedures, using microbiological reports and antibiotic prescriptions as proxy measures of infection.

Introduction

Reports of outbreaks and incidents in the published literature suggest a possible risk of cross-infection following medical procedures that involve the use of semi-invasive ultrasound probes (SIUPs).[1] This risk concerns endocavitary ultrasound probes: transoesophageal echocardiography (TOE) probes, transvaginal (TV) probes and transrectal (TR) probes; as well as non-endocavitary ultrasound probes when in contact with broken skin. Following one particular incident, the UK Medicines and Healthcare products Regulatory Agency (MHRA) released a Medical Device Alert in June 2012 in relation to the decontamination of SIUPs after the death of a patient from hepatitis B virus infection – an event that may have been caused by the failure to appropriately disinfect a TOE probe between each patient use.[2] This event underscores the clinical importance of establishing the infectious risk of semi-invasive ultrasound procedures to support appropriate methods of probe decontamination.

There have been six published outbreaks of healthcare-associated infections related to the use of TOE probes since 2003: in the USA,[3 4] Japan,[5 6] France[7] and Switzerland.[8] These reports included cases of bloodstream infection and pneumonia, associated with *Pseudomonas aeruginosa* and *Legionella pneumophila*, respectively, as well as positive cultures of *Enterobacter cloacae*, *Escherichia coli*, *Serratia marcescens* and *Salmonella enterica* serotype Isangi. Typically, the outbreaks were linked to the use of damaged probes, low-level disinfection or contaminated rinse water. There have been no published outbreaks associated with TV or TR ultrasound probes, although these procedures are commonly employed within outpatient settings and are therefore less likely to be identified as such.

Under the Spaulding classification system, endocavitary ultrasound probes that come into contact with mucous membranes and non-endocavitary ultrasound probes that touch broken skin should both be considered as semi-critical items.[9] In April 2016, Health Protection Scotland (HPS) and Health Facilities Scotland (HFS) published joint guidance recommending the use of high-level disinfection for the decontamination of SIUPs.[10] As demonstrated by a national survey carried out in 2012, prior to national guidance being issued there was considerable variation in practice with regard to methods for cleaning SIUPs in Scotland.[11] Of the 42 departments that responded, only four (9.5%) departments were using high-level disinfection. Similarly, a Europe-wide survey distributed via the European Society of Radiology in 2015 found that only 14.7% of respondents reported using high-level disinfection for endocavitary probes.[12]

This study aimed to use both microbiological and prescribing data as proxy measures to give an estimated risk of infection following SIUP procedures in Scotland from 2010 to 2016, prior to the publication of national HPS guidance in April 2016 on decontamination of SIUPs.

Methods

Data sources

Patient-level data on hospitalisation and procedures were obtained from the National Services Scotland (NSS) General/Acute Inpatient and Day Case dataset (SMR01) and Outpatient Attendance dataset (SMR00).[13] Positive microbiological reports were retrieved from the NSS Electronic Communication of Surveillance in Scotland (ECOSS) dataset, which contains details of micro-organisms and infections identified and reported by microbiology laboratories in the National Health Service (NHS) in Scotland.[14] Antibiotic prescriptions were identified from the NSS Prescribing Information System (PIS), which contains details of all NHS medications prescribed and dispensed in the community in Scotland.[15] Study data were generated during routine care and had all patient identifiers removed prior to analysis. Data were linked using the Community Health Index (CHI) number – a unique patient identifier used in the NHS.[16] NSS Privacy Advisory Committee approval was granted and all data linkage and analysis adhered to NSS Information Governance Policy and Procedures.

Cohort identification

The study created three retrospective cohorts – Cardiology, Gynaecology and Urology – covering the period 2010 to 2016 in Scotland. The study cohorts were identified from SMR01 and SMR00 datasets. Individuals were assigned to one of these cohorts, based on their exposure to certain procedures or hospital episodes/outpatient attendance in selected specialties (Table 1), and who were also Scottish residents aged $\geq$16 as of 1st April 2010 with a valid CHI. Patients were included in the Cardiology cohort if they had undergone a TOE procedure in the period from 1st April 2010 to 31st March 2016 or if they were a Cardiology

inpatient or outpatient in the same time period. Patients were included in the Gynaecology cohort if they had a Gynaecology inpatient/day-case episode or an outpatient attendance under the Gynaecology specialty, and they were included in the Urology cohort if they had a Urology inpatient/day-case episode or an outpatient attendance under the Urology specialty. Due to the lack of recording as to which devices had been used, a number of procedures were assumed to have involved the use of a TV or TR probe, based upon the authors' knowledge of current best practice for medical procedures (Table 1).

[Table 1]

Data extraction

Following cohort identification, patient-level data for individuals assigned to one of the three cohorts were extracted from the data sources. Inpatient/day-case hospital episodes and outpatient attendance, including date of SIUP procedure, were obtained from SMR01 and SMR00 datasets, respectively. For individuals in each of the three cohorts, corresponding ECOSS data were extracted to include all microbiological reports of the following specimens: blood, upper respiratory and lower respiratory specimens for Cardiology specialty attendance/episodes; urine and genital specimens for Gynaecology specialty attendance/episodes; and blood, urine, genital and faecal specimens for Urology specialty attendance/episodes. However, data on sensitive infections, such as human immunodeficiency virus and hepatitis C virus, were not extracted in order to minimise the risk of violating patient confidentiality. *Mycobacterium tuberculosis* was excluded from the analysis for having an incubation period greater than 30 days. For individuals in the three cohorts, corresponding PIS data were extracted to include all community antibiotic prescriptions from the legacy British National Formulary (BNF) Chapter 5.1, Antibacterial

Drugs, excluding anti-tuberculosis drugs and anti-leprotic drugs (paragraphs 9 and 10, respectively). For Gynaecology specialty attendance/episodes, prescriptions were further classified into those agents most commonly used in the treatment of urinary tract infections in Scotland: trimethoprim, nitrofurantoin, ciprofloxacin, cefalexin and co-amoxiclav. Antibiotics prescribed within 30 days of a previous prescription were assumed to be related to the same period of infection and only the first prescription was counted in this period.

From SMR01 data, a Charlson co-morbidity score was calculated, based on the weightings outlined by Charlson et al.[17] and using the algorithm defined for the International Classification of Diseases-10 (ICD-10) codes by Quan et al.[18] Diagnostic codes from hospital admissions in the five years prior to 1st April 2010 were used to calculate the Charlson score. Individuals with no admissions in this period were assigned a score as unknown. SMR01 data were also used to determine the number of hospital stays the patient had in the 12 months prior to 1st April 2010. The number of drug classes, defined as the total number of medicines prescribed from different paragraphs of the legacy BNF in the 12 months prior to 1st April 2010, was used as an additional measure of co-morbidity.[19] SMR01 and PIS datasets were used to identify if a patient was admitted to hospital from a care home location (i.e. a long-term care facility in the community providing a supported care environment) in the 12 months prior to 1st April 2010, or if the patient was registered on the PIS dataset as being in a care home at the time of a prescription in the 12 months prior to the beginning of the study. This implies a patient was resident in a care home at some point in the 12 months prior to the start of the study and should not be interpreted as the patient being resident at the time of any possible infection.

Data linkage and analysis

Corresponding microbiological and prescribing data were linked to SIUP procedures using the unique patient CHI number within the NHS Scotland Infection Intelligence Platform (IIP).[20] For both microbiological reports and antibiotic prescriptions, a positive outcome linked to a SIUP procedure was defined as a report or prescription in the period from one day following the procedure date to 30 days following the procedure. The 30-day period was chosen on the basis of standard incubation periods for micro-organisms that are likely to pose a risk of cross-infection via SIUPs, as a 'worst-case' scenario.[21] Individuals in each cohort contributed person-time follow-up to the unexposed grouping whilst not exposed to a SIUP, starting from the date they entered the cohort (1st April 2010). Individuals exposed to a SIUP procedure contributed person-time follow-up to the exposed group from one day to 30 days post-procedure. All individuals were followed-up until the end of the study (31st March 2016) or date of death, if applicable. Cox proportional hazards was used to compare the rate of occurrence of the appropriate outcome (i.e. positive microbiological report or antibiotic prescription) in the cohort for the exposed period for each type of SIUP procedure against the non-exposed period, to determine the hazard ratio and 95% confidence interval. This process was performed independently for both microbiological and prescribing outcomes. Unadjusted and fully adjusted analyses were conducted for the following factors: age, gender, NHS board of residence, Charlson co-morbidity score, number of hospital admissions in past 12 months, number of BNF drug classes prescribed in past 12 months and care home residence in past 12 months. A p-value of ≤ 0.05 was chosen as the threshold for statistical significance. Data manipulation was carried out in SPSS (IBM, version 21) and all statistical analysis was conducted in R (version 3.2.0) using the survival package.[22]

Results

The number of patients included were 495 786, 330 500 and 156 625 for the Cardiology, Gynaecology and Urology cohorts, respectively (Table 2). The number of SIUP procedures recorded were 3 364 for TOE, 60 698 for TV ultrasound and 15 934 for TR ultrasound. For ECOSS reports, the total number of person-years follow-up was 72 805 743, 53 723 455 and 24 850 921 for Cardiology, Gynaecology and Urology cohorts, respectively. For PIS prescriptions, the total number of person-years follow-up was 72 811 440, 53 723 480 and 24 850 921 for the same cohorts. The slight difference in person-time follow-up for ECOSS and PIS outcomes was due to variation in the number of individuals with a date of death prior to the positive outcome (i.e. microbiological reports could be submitted after date of death).

[Table 2]

Of the Cardiology cohort, 51.6% were male, 27.9% had previously been hospitalised and 1.1% had been resident in a care home. For the Gynaecology cohort, 16.2% had previously been hospitalised and 0.1% had been resident in a care home; as for the Urology cohort, 23.8% had been hospitalised and 0.6% had been resident in a care home. In addition, 12.3% of the Cardiology cohort, 19.2% of the Gynaecology cohort and 22.4% of the Urology cohort had not been prescribed any drugs within the past 12 months. Twenty-seven percent of the Cardiology cohort had a Charlson score of 1 or higher, as did 7.0% of the Gynaecology cohort and 18.6% of the Urology cohort, indicating that the cohorts were relatively healthy. Both the Cardiology and Urology cohorts had a higher prevalence of co-morbidities than the Gynaecology cohort, in addition to which the Gynaecology cohort was largely younger in age. For example, 64.9% of the Gynaecology cohort was below the age of 45, whereas

71.1% of the Cardiology cohort and 58.1% of the Urology cohort were aged 55 years or older.

The 30-day incidence rate per 100 000 person-years (p100,000py) of positive microbiological reports was raised for those exposed to each type of SIUP procedure, compared to those not exposed – TOE exposed 310.90 vs. 63.66 p100,000py; TV exposed 138.88 vs. 86.13 p100,000py; and TR exposed 494.27 vs. 134.12 p100,000py (Table 3). Similarly, the 30-day incidence rate of community antibiotic prescriptions was raised – TOE exposed 3497.05 vs. 3250.43 p100,000py; TV exposed 4039.94 vs. 2899.51 p100,000py; and TR exposed 4958.81 vs. 2704.94 p100,000py. There was a significant increase (p<0.001) in the unadjusted risk of infection for all three types of SIUP procedure, as determined by positive microbiological reports and community antibiotic prescriptions.

The increased risk continued to be statistically significant when the analysis was adjusted for confounding factors. A greater adjusted hazard ratio (HR) of positive microbiological reports was observed for patients who had undergone TOE (HR: 4.92; 95% CI: 3.17–7.63; p<0.001), TV (HR: 1.41; 95% CI: 1.21–1.64; p<0.001) and TR ultrasound (HR: 3.40; 95% CI: 2.90–3.99; p<0.001). Similarly, there was a greater adjusted HR of community antibiotic prescribing for those who had received TV (HR: 1.26; 95% CI: 1.20–1.32; p<0.001) and TR (HR: 1.75; 95% CI: 1.66–1.84; p<0.001) ultrasound. The adjusted HR for community antibiotic prescriptions following TOE procedures was not found to be significant (HR: 1.05; 95% CI: 0.92–1.20; p=0.49).

[Table 3]

Discussion

Through linking national datasets of routinely collected data, we found that exposure to a SIUP procedure was associated with an increased risk of infection, as demonstrated by raised hazard ratios for both positive microbiological reports and community antibiotic prescriptions. To the authors' knowledge, this is the first study using linkage of national datasets to determine the risk of infection associated with SIUP procedures.

Whilst a range of studies have measured the prevalence of contamination on SIUPs,[23-27] few have attempted to assess the risk to patients of cross-infection from re-use of contaminated probes. Bénet et al.[28] conducted a cohort study of 50 244 patients tested for human immunodeficiency virus (HIV) and 105 955 patients tested for hepatitis C virus (HCV), between 2004 and 2012, in a single university hospital (Lyon, France). Multivariate logistic regression models were adjusted for sex, age and time period, to calculate the prevalence of HIV and HCV seropositivity. These established that exposure to a SIUP in the past 12 months was not associated with an increased risk of seropositivity for HIV (p=0.18) or HCV (p=0.43). In a subgroup Cox model analysis of 13 730 and 8232 patients tested for HCV and HIV, the incidence of seroconversion was 16.1 and 0 cases per 10 000 patient-years, respectively, among patients with exposure to a SIUP in the 12 months before testing. The incidence of HIV and HCV seroconversion did not significantly differ according to probe exposure (p=0.64 and p=0.69). However, fewer than 2000 patients in the full cohort were exposed to SIUPs (cf. approx. 80 000 procedures in our study), and the authors did not distinguish between TOE, TV and TR ultrasound procedures when reporting incidence rates. In contrast, our study used larger cohorts (approx. 150 000 to 500 000) distributed across an entire country, including hospitals with different infection rates and decontamination practices. This

feature, together with the tendency of bacteria to persist on inanimate surfaces for a longer period of time than viruses,[29] might explain why our results demonstrated a significantly increased risk, whereas the results of Bénet et al. did not.

The incidence rates calculated from our study are consistent with the risk of infection estimated by other published studies, and indicate an increase in absolute risk of 0.05–2.25% attributable to SIUP exposure. For example, Leroy et al.[30] predicted a cross-infection risk for TV and TR probes of 0.7–6.0% for selected microbial pathogens, including blood-borne viruses, human papillomavirus and *Chlamydia trachomatis*, based on modelling for a hypothetical cohort of four million procedures. These risks were based upon estimated parameters acquired from published literature. A meta-analysis of 24 cohort studies (total of 24 627 patients) has pooled the prevalence of infectious complications following TR ultrasound-guided prostate biopsy, indicating an infection risk of 3.1%.[31] Both studies have been criticised for methodological limitations addressed by our study through the inclusion of a multi-site cohort and use of real surveillance data.[32 33]

Adjusted hazard ratios were greatest for those undergoing TOE procedures, followed by TR ultrasound procedures. The substantially greater hazard ratio for TOE procedures reflects the number of infection outbreaks associated with TOE probes in the published literature.[3-8] These patients commonly receive ultrasound examination during an episode of care as an inpatient and are likely to be medically compromised with multiple co-morbidities, increasing their risk of infection. Therefore, we made statistical adjustments to minimise the impact of medical co-morbidities as a confounding factor. Since infective endocarditis is a frequent indication for TOE procedures, patients with positive blood cultures or antibiotic prescriptions in the 30 days before the procedure were excluded from analysis. TOE probes

are commonly used as an operative aid during cardiac surgery – a situation that would be expected to heighten the risk of infection – however, we were unable to distinguish between critical and non-critical situations using our data sources.

Limitations

The use of routinely collected data inevitably entailed a number of limitations, such as precluding the use of patient-specific data on SIUP decontamination methods; although, it allowed the use of larger cohorts than would normally be available for analysis. Positive microbiological reports and antibiotic prescriptions are only proxy measures for clinical infection and may respectively represent asymptomatic colonisation – as opposed to overt infection – or a provisional diagnosis of infection without prior confirmation by microbiological culture. Reporting of urine, genital and faecal specimens in ECOSS is not mandatory and, since there was significant variation amongst NHS regional boards in specimen reporting, this indicates that the infection risk may be under-estimated. Neither is it mandatory to record SIUP procedures for inpatients and day-cases unless the patient has been specifically admitted for that procedure; therefore, it is possible that some procedures will not have been identified in the study cohort. The non-significant difference in antibiotic prescriptions for those receiving TOE procedures in the Cardiology cohort is likely to be due to these patients undergoing the procedure during an inpatient stay, with the consequence that any antibiotic prescriptions will not be recorded in the PIS community prescribing dataset. Hospital inpatient prescribing is not currently available as a national dataset. Pre-surgical antibiotic prophylaxis for needle biopsy of the prostate is recommended by the European Association of Urology[34] and the American Urological Association,[35] and this practice could have lowered the infection risk following TR ultrasound.

Clinical relevance

Existing guidelines from HPS,[10] the Centers for Disease Control and Prevention,[9] the American Institute of Ultrasound in Medicine,[36] the Australasian Society for Ultrasound in Medicine/Australasian College for Infection Prevention and Control,[37] the British Society of Echocardiography[38] and the World Federation for Ultrasound in Medicine and Biology,[39] all recommend that high-level disinfection is applied for SIUPs, even if a barrier sheath or protective cover is used, irrespective of procedure type. This recommendation is based upon the observation that sheaths frequently perforate before or during use. Australian guidelines strictly encourage the use of sheaths for all procedure types, and sterile sheaths for use in critical aseptic fields.[37] In Scotland, as in the USA, current guidelines do not require the use of a sheath unless it is clinically indicated to aid the diagnostic procedure.[10]

Our findings imply that disinfection practices from 2010 to 2016 in Scotland may have been inadequate for the re-use of SIUPs, posing a risk of cross-infection; albeit a very low risk. Under the precautionary principle, in the event that the risk is low and the consequences are high, full scientific certainty should not be used as justification for postponing cost-effective measures to prevent future infections. Hence, failure to comply with existing guidance on disinfection of SIUPs will continue to result in an unacceptable risk of harm to patients.

Implications for research

Future research in this area should initially focus on the reasons for non-compliance with national guidance on SIUP decontamination and subsequent evaluation of guideline

implementation to determine whether changes in practice are widely adopted and sustained. Following this, a prospective cohort study using a similar methodology should be conducted to ascertain if national guidance recommending high-level disinfection has reduced the risk of infection from SIUP procedures. Ideally, the recording of all SIUP procedures in the SMR datasets should become mandatory, which would ensure that data are more robust for any future data linkage exercises or national surveillance. Local surveillance of infections following SIUP procedures would facilitate the identification of future outbreaks, allowing researchers to determine the risk of infection from SIUP exposure using clinically confirmed diagnoses.

Conclusion

Analysis of linked national datasets demonstrated a greater risk of positive microbiological reports and community antibiotic prescriptions within 30 days for adults who had undergone SIUP procedures in Scotland. This finding indicates that, prior to the publication in April 2016 of national HPS guidance advocating high-level disinfection, the re-use of SIUPs posed an increased risk of infection.

References

1. Koibuchi H, Kotani K and Taniguchi N. Ultrasound probes as a possible vector of bacterial transmission. *Med Ultrason* 2013; 15: 41–44.
2. Medicines and Healthcare products Regulatory Agency. Medical Device Alert: Reusable transoesophageal echocardiography, transvaginal and transrectal ultrasound probes (transducers) (MDA/2012/037), https://assets.digital.cabinet-office.gov.uk/media/5485abf1ed915d4c0d000261/con160567.pdf (2012, accessed 2 January 2018).
3. Bancroft EA, English L, Terashita D, et al. Outbreak of *Escherichia coli* infections associated with a contaminated transesophageal echocardiography probe. *Infect Control Hosp Epidemiol* 2013; 34: 1121–1123.
4. Suleyman G, Tibbetts R, Perri MB, et al. Nosocomial outbreak of a novel extended-spectrum β-lactamase *Salmonella enterica* serotype Isangi among surgical patients. *Infect Control Hosp Epidemiol* 2016; 37: 954–961.
5. Seki M, Machida H, Yamagishi Y, et al. Nosocomial outbreak of multidrug-resistant *Pseudomonas aeruginosa* caused by damaged transesophageal echocardiogram probe used in cardiovascular surgical operations. *J Infect Chemother* 2013; 19: 677–681.
6. Kanemitsu K, Endo S, Oda K, et al. An increased incidence of *Enterobacter cloacae* in a cardiovascular ward. *J Hosp Infect* 2007; 66: 130–134.
7. Levy PY, Teysseire N, Etienne J, et al. A nosocomial outbreak of *Legionella pneumophila* caused by contaminated transesophageal echocardiography probes. *Infect Control Hosp Epidemiol* 2003; 24: 619–622.

8. Vetter L, Schuepfer G, Kuster SP, et al. A hospital-wide outbreak of *Serratia marcescens* and Ishikawa's "fishbone" analysis to support outbreak control. *Qual Manag Health Care* 2016; 25: 1–7.
9. Centers for Disease Control and Prevention. Guideline for Disinfection and Sterilization in Healthcare Facilities, https://www.cdc.gov/infectioncontrol/pdf/guidelines/disinfection-guidelines.pdf (2008, accessed 2 January 2018).
10. Health Protection Scotland. NHSScotland Guidance for Decontamination of Semi-Critical Ultrasound Probes; Semi-Invasive and Non-Invasive Ultrasound Probes, http://www.hps.scot.nhs.uk/resourcedocument.aspx?id=5729 (2017, accessed 2 January 2018).
11. Health Facilities Scotland. Report on the 2012 National Survey of the Decontamination of Transoesophageal Echocardiography, Transvaginal and Transrectal Ultrasound Probes. Unpublished report, 2015.
12. Nyhsen CM, Humphreys H, Nicolau C, et al. Infection prevention and ultrasound probe decontamination practices in Europe: a survey of the European Society of Radiology. *Insights Imaging* 2016; 7: 841–847.
13. Information Services Division Scotland. The National Data Catalogue, http://www.ndc.scot.nhs.uk/ (accessed 2 January 2018).
14. Health Protection Scotland. ECOSS (The Electronic Communication of Surveillance in Scotland), http://www.hps.scot.nhs.uk/surveillance/SystemsDetail.aspx?id=248 (accessed 2 January 2018).
15. Alvarez-Madrazo S, McTaggart S, Nangle C, et al. Data resource profile: the Scottish national Prescribing Information System (PIS). *Int J Epidemiol* 2016; 45: 714–715f.

16. Information Services Division Scotland. Data Dictionary A-Z: CHI Number, http://www.ndc.scot.nhs.uk/Dictionary-A-Z/Definitions/index.asp?ID=128&Title=CHI%20Number (accessed 2 January 2018).
17. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40: 373–383.
18. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005; 43: 1130–1139.
19. MedicinesComplete. British National Formulary (BNF) Legacy, https://www.medicinescomplete.com/mc/bnflegacy/64/ (accessed 2 January 2018).
20. Bennie M, Malcolm W, Marwick CA, et al. Building a national Infection Intelligence Platform to improve antimicrobial stewardship and drive better patient outcomes: the Scottish experience. *J Antimicrob Chemother* 2017; 72: 2938–2942.
21. Heymann DL. *Control of Communicable Diseases Manual*. Geneva: World Health Organization, 2004.
22. Therneau T. A Package for Survival Analysis in S. version 2.38, https://cran.r-project.org/web/packages/survival/index.html (2015, accessed 2 January 2018).
23. Kuwata T, Takahashi H, Koibuchi H, et al. Incidence of human papillomavirus contamination of transvaginal probes in Japan and possible contamination prevention strategy. *J Med Ultrasonics* 2016; 43: 505–508.
24. Buescher DL, Möllers M, Falkenberg MK, et al. Disinfection of transvaginal ultrasound probes in a clinical setting: comparative performance of automated and manual reprocessing methods. *Ultrasound Obstet Gynecol* 2016; 47: 646–651.

25. Ngu A, McNally G, Patel D, et al. Reducing transmission risk through high-level disinfection of transvaginal ultrasound transducer handles. *Infect Control Hosp Epidemiol* 2015; 36: 581–584.
26. M'Zali F, Bounizra C, Leroy S, et al. Persistence of microbial contamination on transvaginal ultrasound probes despite low-level disinfection procedure. *PLoS ONE* 2014; 9: e93368.
27. Casalegno J, Carval KLB, Eibach D, et al. High risk HPV contamination of endocavity vaginal ultrasound probes: an underestimated route of nosocomial infection? *PLoS ONE* 2012; 7: e48137.
28. Bénet T, Ritter J, Vanhems P. Risk of human immunodeficiency virus and hepatitis C virus infection related to endocavitary ultrasound probe expsoure in France. *Infect Control Hosp Epidemiol* 2014; 35: 1429–1431.
29. Kramer A, Schwebke I, Kampf G. How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. *BMC Infect Dis* 2006; 6: 130.
30. Leroy S, M'Zali F, Kann M, et al. Impact of vaginal-rectal ultrasound examinations with covered and low-level disinfected transducers on infectious transmissions in France. *Infect Control Hosp Epidemiol* 2014; 35: 1497–1504.
31. Leroy S. Infectious risk of endovaginal and transrectal ultrasonography: systematic review and meta-analysis. *J Hosp Infect* 2013; 83: 99–106.
32. Bénet T, Vanhems P. Methodological issues concerning the meta-analysis by Leroy on the risk of infectious complications after endovaginal and transrectal ultrasonography. *J Hosp Infect* 2014; 88: 52–53.
33. Bénet T, Ecochard R, Vanhems P. Letter to the editor regarding "Impact of vaginal-rectal ultrasound examinations with covered and low-level disinfected transducers

on infectious transmissions in France" by Leroy et al. *Infect Control Hosp Epidemiol* 2015; 36: 851–852.

34. Heidenreich A, Bastian PJ, Bellmunt J, et al. EAU guidelines on prostate cancer. Part 1: Screening, diagnosis and local treatment with curative intent – update 2013. *Eur Urol* 2014; 65: 124–137.
35. Wolf JS, Bennett CJ, Dmochowski RR, et al. Best practice policy statement on urologic surgery antimicrobial prophylaxis. *J Urol* 2008; 179: 1379–1390.
36. American Institute of Ultrasound in Medicine. Guidelines for Cleaning and Preparing External- and Internal-Use Ultrasound Probes Between Patients, Safe Handling, and Use of Ultrasound Coupling Gel, http://www.aium.org/officialStatements/57 (2017, accessed 13 February 2018).
37. Australasian Society for Ultrasound in Medicine, Australasian College for Infection Prevention and Control. Guidelines for Reprocessing Ultrasound Transducers. *AJUM* 2017; 20: 30–40.
38. Kanagala P, Bradley C, Hoffman P, et al. Guidelines for transoesophageal echocardiographic probe cleaning and disinfection from the British Society of Echocardiography. *Eur J Echocardiogr* 2011; 12: i17–23.
39. Abramowicz JS, Evans DH, Fowlkes JB, et al. Guidelines for cleaning transvaginal ultrasound transducers between patients. *Ultrasound Med Biol* 2017; 43: 1076–1079.

Table 1: Inclusion criteria for Cardiology, Gynaecology and Urology cohorts.

Cardiology cohort Inclusion criteria: • Cardiology inpatient/day-case episode; General Medicine inpatient/day-case episode with Cardiology diagnosis code (ICD10 I20-I25, I26-I28, I30-I52); Cardiology outpatient attendance; or procedure code U20.2 Transoesophageal echocardiography Exposure classed as procedure code: • U20.2 Transoesophageal echocardiography
Gynaecology cohort Inclusion criteria: • Gynaecology inpatient/day-case episode or outpatient attendance Exposure classed as procedure code: • Q55.5 Transvaginal ultrasound examination of female genital tract • Q51.5 Transvaginal ultrasound guided aspiration of ovarian cyst • Q21 Placement/removal of IUD AND U09.2 Ultrasound of pelvis • Q48.4 Transvaginal oocyte recovery • Q55.9 Unspecified examination of female genital tract AND U09.2 Ultrasound of pelvis
Urology cohort Inclusion criteria: • Urology inpatient/day-case episode or outpatient attendance Exposure classed as procedure code: • M70.3 Rectal needle biopsy of prostate • M70.6 Radioactive seed implantation into prostate

Table 2: Characteristics of Cardiology, Gynaecology and Urology cohorts by age group, gender, Charlson score, British National Formulary (BNF) drug classes prescribed, previous hospital admissions and past care home residence.

	Cardiology Cohort		Gynaecology Cohort		Urology Cohort	
	n	%	n	%	n	%
Age group						
16-24	12 271	2.5	70 698	21.4	9 142	5.8
25-34	17 747	3.6	75 033	22.7	13 999	8.9
35-44	38 756	7.8	68 607	20.8	19 272	12.3
45-54	74 527	15.0	55 645	16.8	23 151	14.8
55-64	101 783	20.5	28 385	8.6	33 054	21.1
65-74	116 368	23.5	19 674	6.0	33 470	21.4
75-84	100 322	20.2	10 497	3.2	20 401	13.0
≥85	34 012	6.9	1 961	0.6	4 136	2.6
Gender						
Male	256 031	51.6	0	0.0	156 625	100.0
Female	239 750	48.4	330 500	100.0	0	0.0
Charlson score						
0	168 085	33.9	121 025	36.6	53 653	34.3
1-2	99 945	20.2	19 765	6.0	22 004	14.1
3-4	24 206	4.9	1 866	0.6	4 980	3.2
≥5	9 560	1.9	1 303	0.4	1 993	1.3
Unknown	193 990	39.1	186 541	56.4	73 995	47.2
BNF drug classes prescribed						
0	60 778	12.3	63 476	19.2	35 092	22.4
1-4	134 104	27.1	159 761	48.3	56 371	36.0
5-9	162 250	32.7	74 959	22.7	40 933	26.1
10-14	94 938	19.2	23 444	7.1	17 682	11.3
15-19	33 538	6.8	6 816	2.1	5 135	3.3
≥20	10 178	2.1	2 044	0.6	1 412	0.9
Previous hospital admissions						
0	357 476	72.1	276 927	83.8	119 320	76.2
1	83 053	16.8	39 005	11.8	22 167	14.2
2	30 531	6.2	9 133	2.8	7 993	5.1
3	12 312	2.5	2 734	0.8	3 409	2.2
≥4	12 414	2.5	2 701	0.8	3 736	2.4
Past care home residence						
No	490 478	98.9	330 093	99.9	155 718	99.4
Yes	5 308	1.1	407	0.1	907	0.6

Table 3: Unadjusted and adjusted hazard ratios (HR), with 95% confidence intervals (CI) and *p*-values, for Electronic Communication of Surveillance in Scotland (ECOSS) positive microbiological reports and Prescribing Information System (PIS) community antibiotic prescriptions by transoesophageal echocardiography (TOE), transvaginal (TV) and transrectal (TR) ultrasound procedures.

		Number of events	Total person-years	Incidence rate per 100 000 person-years	Unadjusted			Adjusted		
					HR (95% CI)		*p*-value	HR (95% CI)		*p*-value
ECOSS reports										
Cardiology	*No procedure*	46 343	72 799 310	63.66	1.00	Reference		1.00	Reference	
	TOE procedure	20	6 433	310.90	4.64	(95% CI: 3.00 – 7.20)	<0.001	4.92	(95% CI: 3.17 – 7.63)	<0.001
Gynaecology	*No procedure*	46 167	53 602 489	86.13	1.00	Reference		1.00	Reference	
	TV procedure	168	120 967	138.88	1.40	(95% CI: 1.20 – 1.63)	<0.001	1.41	(95% CI: 1.21 – 1.64)	<0.001
Urology	*No procedure*	33 289	24 819 966	134.12	1.00	Reference		1.00	Reference	
	TR procedure	153	30 955	494.27	3.36	(95% CI: 2.87 – 3.94)	<0.001	3.40	(95% CI: 2.90 – 3.99)	<0.001
PIS prescriptions										
Cardiology	*No procedure*	2 366 475	72 805 006	3250.43	1.00	Reference		1.00	Reference	
	TOE procedure	225	6 434	3497.05	0.99	(95% CI: 0.86 – 1.12)	0.827	1.05	(95% CI: 0.92 – 1.20)	0.490
Gynaecology	*No procedure*	1 554 212	53 602 513	2899.51	1.00	Reference		1.00	Reference	
	TV procedure	4 887	120 967	4039.94	1.40	(95% CI: 1.34 – 1.47)	<0.001	1.26	(95% CI: 1.20 – 1.32)	<0.001
Urology	*No procedure*	671 366	24 819 966	2704.94	1.00	Reference		1.00	Reference	
	TR procedure	1 535	30 955	4958.81	1.67	(95% CI: 1.59 – 1.76)	<0.001	1.75	(95% CI: 1.66 – 1.84)	<0.001

Table 4 (Supplemental): Cardiology cohort hazard ratios for ECOSS microbiological reports and PIS antibiotic prescriptions by all variables.

Variable	ECOSS reports				PIS prescriptions			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	HR (95% CI)		HR (95% CI)	*p*-value	HR (95% CI)		HR (95% CI)	*p*-value
Procedure								
No	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
Yes	4.64	(95% CI: 3.00 – 7.20)	4.92	(95% CI: 3.17 – 7.63)	<0.001	0.99	(95% CI: 0.86 – 1.12)	1.05	(95% CI: 0.92 – 1.20)	0.490
Age group								
16-24	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
25-34	1.60	(95% CI: 1.40 – 1.83)	1.42	(95% CI: 1.24 – 1.62)	<0.001	1.03	(95% CI: 1.02 – 1.05)	0.95	(95% CI: 0.94 – 0.96)	<0.001
35-44	1.80	(95% CI: 1.60 – 2.03)	1.33	(95% CI: 1.17 – 1.50)	<0.001	1.12	(95% CI: 1.11 – 1.13)	0.92	(95% CI: 0.91 – 0.93)	<0.001
45-54	2.49	(95% CI: 2.22 – 2.80)	1.50	(95% CI: 1.33 – 1.68)	<0.001	1.22	(95% CI: 1.21 – 1.24)	0.88	(95% CI: 0.87 – 0.89)	<0.001
55-64	4.03	(95% CI: 3.60 – 4.52)	2.00	(95% CI: 1.78 – 2.24)	<0.001	1.41	(95% CI: 1.40 – 1.42)	0.89	(95% CI: 0.88 – 0.90)	<0.001
65-74	5.39	(95% CI: 4.81 – 6.03)	2.25	(95% CI: 2.01 – 2.52)	<0.001	1.63	(95% CI: 1.61 – 1.64)	0.88	(95% CI: 0.87 – 0.89)	<0.001
75-84	5.36	(95% CI: 4.79 – 6.00)	2.11	(95% CI: 1.88 – 2.37)	<0.001	1.72	(95% CI: 1.70 – 1.74)	0.86	(95% CI: 0.85 – 0.87)	<0.001
≥85	5.33	(95% CI: 4.75 – 5.99)	2.20	(95% CI: 1.96 – 2.48)	<0.001	1.84	(95% CI: 1.82 – 1.86)	0.90	(95% CI: 0.89 – 0.91)	<0.001
Gender								
Male	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
Female	0.90	(95% CI: 0.89 – 0.92)	0.77	(95% CI: 0.76 – 0.79)	<0.001	1.53	(95% CI: 1.53 – 1.53)	1.32	(95% CI: 1.32 – 1.32)	<0.001
Charlson score								
0	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
1-2	2.45	(95% CI: 2.39 – 2.51)	1.61	(95% CI: 1.57 – 1.65)	<0.001	1.35	(95% CI: 1.35 – 1.35)	1.04	(95% CI: 1.04 – 1.04)	<0.001
3-4	3.58	(95% CI: 3.46 – 3.70)	1.74	(95% CI: 1.68 – 1.80)	<0.001	1.59	(95% CI: 1.58 – 1.60)	1.05	(95% CI: 1.04 – 1.06)	<0.001
≥5	4.63	(95% CI: 4.43 – 4.85)	2.00	(95% CI: 1.91 – 2.10)	<0.001	1.66	(95% CI: 1.65 – 1.68)	1.06	(95% CI: 1.05 – 1.07)	<0.001
Unknown	0.76	(95% CI: 0.74 – 0.78)	1.04	(95% CI: 1.01 – 1.07)	0.005	0.68	(95% CI: 0.68 – 0.69)	0.90	(95% CI: 0.90 – 0.90)	<0.001
BNF drug classes prescribed								
0	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference

1-4	1.39	(95% CI: 1.32 – 1.46)	1.28	(95% CI: 1.21 – 1.34)	<0.001	1.82	(95% CI: 1.81 – 1.84)	1.72	(95% CI: 1.71 – 1.73)	<0.001
5-9	2.79	(95% CI: 2.66 – 2.93)	2.07	(95% CI: 1.97 – 2.18)	<0.001	2.80	(95% CI: 2.78 – 2.82)	2.56	(95% CI: 2.54 – 2.57)	<0.001
10-14	5.16	(95% CI: 4.92 – 5.42)	3.31	(95% CI: 3.15 – 3.49)	<0.001	4.28	(95% CI: 4.25 – 4.31)	3.74	(95% CI: 3.71 – 3.76)	<0.001
15-19	8.75	(95% CI: 8.33 – 9.20)	5.02	(95% CI: 4.75 – 5.30)	<0.001	6.07	(95% CI: 6.03 – 6.11)	5.08	(95% CI: 5.05 – 5.12)	<0.001
≥20	14.16	(95% CI: 13.4 – 15.0)	7.32	(95% CI: 6.89 – 7.79)	<0.001	8.14	(95% CI: 8.07 – 8.21)	6.58	(95% CI: 6.52 – 6.64)	<0.001
Previous hospital admissions										
0	1.00	Reference	1.00	Reference		1.00	Reference	1.00	Reference	
1	1.69	(95% CI: 1.66 – 1.73)	1.06	(95% CI: 1.03 – 1.09)	<0.001	1.41	(95% CI: 1.41 – 1.41)	1.01	(95% CI: 1.01 – 1.02)	<0.001
2	2.25	(95% CI: 2.18 – 2.33)	1.12	(95% CI: 1.08 – 1.16)	<0.001	1.62	(95% CI: 1.61 – 1.63)	1.02	(95% CI: 1.02 – 1.03)	<0.001
3	2.93	(95% CI: 2.80 – 3.05)	1.22	(95% CI: 1.17 – 1.28)	<0.001	1.81	(95% CI: 1.79 – 1.82)	1.03	(95% CI: 1.03 – 1.04)	<0.001
≥4	4.66	(95% CI: 4.50 – 4.83)	1.69	(95% CI: 1.62 – 1.76)	<0.001	2.02	(95% CI: 2.01 – 2.04)	1.08	(95% CI: 1.07 – 1.09)	<0.001
Past care home residence										
No	1.00	Reference	1.00	Reference		1.00	Reference	1.00	Reference	
Yes	1.99	(95% CI: 1.83 – 2.16)	1.02	(95% CI: 0.94 – 1.11)	0.615	1.81	(95% CI: 1.78 – 1.83)	1.20	(95% CI: 1.19 – 1.22)	<0.001
NHS board of residence										
GG&C	1.00	Reference	1.00	Reference		1.00	Reference	1.00	Reference	
A&A	1.24	(95% CI: 1.19 – 1.28)	1.13	(95% CI: 1.10 – 1.17)	<0.001	0.99	(95% CI: 0.99 – 1.00)	0.99	(95% CI: 0.99 – 1.00)	0.003
Borders	0.81	(95% CI: 0.76 – 0.87)	0.87	(95% CI: 0.82 – 0.93)	<0.001	0.85	(95% CI: 0.84 – 0.86)	0.95	(95% CI: 0.94 – 0.96)	<0.001
D&G	1.14	(95% CI: 1.08 – 1.20)	1.11	(95% CI: 1.05 – 1.16)	0.001	0.89	(95% CI: 0.88 – 0.89)	0.94	(95% CI: 0.93 – 0.95)	<0.001
Fife	0.94	(95% CI: 0.90 – 0.98)	0.93	(95% CI: 0.89 – 0.97)	<0.001	0.91	(95% CI: 0.90 – 0.91)	0.95	(95% CI: 0.95 – 0.96)	<0.001
Forth Valley	1.18	(95% CI: 1.13 – 1.24)	1.21	(95% CI: 1.15 – 1.26)	<0.001	0.93	(95% CI: 0.92 – 0.94)	0.97	(95% CI: 0.96 – 0.98)	<0.001
Grampian	0.87	(95% CI: 0.84 – 0.91)	0.89	(95% CI: 0.85 – 0.92)	<0.001	0.92	(95% CI: 0.91 – 0.92)	1.00	(95% CI: 1.00 – 1.01)	0.021
Highland	0.84	(95% CI: 0.80 – 0.88)	0.86	(95% CI: 0.82 – 0.90)	<0.001	0.84	(95% CI: 0.84 – 0.85)	0.92	(95% CI: 0.91 – 0.92)	<0.001
Lanarkshire	0.95	(95% CI: 0.92 – 0.98)	0.96	(95% CI: 0.93 – 0.99)	0.005	1.04	(95% CI: 1.03 – 1.04)	1.04	(95% CI: 1.04 – 1.05)	<0.001
Lothian	1.17	(95% CI: 1.13 – 1.20)	1.26	(95% CI: 1.22 – 1.30)	<0.001	0.93	(95% CI: 0.93 – 0.94)	1.03	(95% CI: 1.02 – 1.03)	<0.001
Orkney	0.37	(95% CI: 0.30 – 0.47)	0.42	(95% CI: 0.34 – 0.53)	<0.001	0.70	(95% CI: 0.68 – 0.71)	0.84	(95% CI: 0.82 – 0.86)	<0.001
Shetland	0.90	(95% CI: 0.75 – 1.08)	0.89	(95% CI: 0.74 – 1.07)	0.208	0.87	(95% CI: 0.85 – 0.89)	0.95	(95% CI: 0.92 – 0.97)	<0.001
Tayside	1.12	(95% CI: 1.08 – 1.17)	1.19	(95% CI: 1.14 – 1.23)	<0.001	0.91	(95% CI: 0.91 – 0.92)	0.99	(95% CI: 0.98 – 0.99)	<0.001
WI	1.02	(95% CI: 0.88 – 1.17)	0.95	(95% CI: 0.82 – 1.09)	0.440	0.98	(95% CI: 0.97 – 1.00)	0.99	(95% CI: 0.97 – 1.01)	0.451

GG&C = Greater Glasgow & Clyde; A&A = Ayrshire & Arran; D&G = Dumfries & Galloway; WI = Western Isles.

Table 5 (Supplemental): Gynaecology cohort hazard ratios for ECOSS microbiological reports and PIS antibiotic prescriptions by all variables.

Variable	ECOSS reports				PIS prescriptions			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	HR (95% CI)		HR (95% CI)	*p*-value	HR (95% CI)		HR (95% CI)	*p*-value
Procedure								
No	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
Yes	1.40	(95% CI: 1.20– 1.63)	1.41	(95% CI: 1.21 – 1.64)	<0.001	1.40 (95% CI: 1.34 – 1.47)	1.26	(95% CI: 1.20 – 1.32) <0.001
Age group								
16-24	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
25-34	0.85	(95% CI: 0.82 – 0.88)	0.79	(95% CI: 0.77 – 0.82)	<0.001	0.91 (95% CI: 0.90 – 0.91)	0.84	(95% CI: 0.83 – 0.84) <0.001
35-44	1.01	(95% CI: 0.97 – 1.04)	0.85	(95% CI: 0.82 – 0.88)	<0.001	1.00 (95% CI: 0.98 – 1.00)	0.83	(95% CI: 0.83 – 0.84) <0.001
45-54	1.30	(95% CI: 1.26 – 1.35)	1.02	(95% CI: 0.98 – 1.05)	0.290	1.10 (95% CI: 1.09 – 1.11)	0.86	(95% CI: 0.85 – 0.87) <0.001
55-64	2.63	(95% CI: 2.54 – 2.72)	1.68	(95% CI: 1.62 – 1.74)	<0.001	1.56 (95% CI: 1.54 – 1.58)	1.05	(95% CI: 1.04 – 1.06) <0.001
65-74	4.63	(95% CI: 4.48 – 4.78)	2.53	(95% CI: 2.44 – 2.62)	<0.001	2.31 (95% CI: 2.29 – 2.34)	1.30	(95% CI: 1.29 – 1.31) <0.001
75-84	6.63	(95% CI: 6.40 – 6.87)	3.32	(95% CI: 3.20 – 3.46)	<0.001	2.72 (95% CI: 2.69 – 2.75)	1.35	(95% CI: 1.33 – 1.37) <0.001
≥85	10.22	(95% CI: 9.61 – 10.9)	5.00	(95% CI: 4.69 – 5.33)	<0.001	3.32 (95% CI: 3.24 – 3.40)	1.56	(95% CI: 1.53 – 1.60) <0.001
Charlson score								
0	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
1-2	2.26	(95% CI: 2.20 – 2.33)	1.07	(95% CI: 1.04 – 1.10)	<0.001	1.53 (95% CI: 1.52 – 1.54)	0.92	(95% CI: 0.92 – 0.93) <0.001
3-4	4.58	(95% CI: 4.32 – 4.87)	1.29	(95% CI: 1.21 – 1.37)	<0.001	2.17 (95% CI: 2.13 – 2.22)	0.89	(95% CI: 0.87 – 0.91) <0.001
≥5	3.23	(95% CI: 2.96 – 3.53)	1.36	(95% CI: 1.24 – 1.49)	<0.001	1.53 (95% CI: 1.48 – 1.59)	0.87	(95% CI: 0.84 – 0.90) <0.001
Unknown	0.59	(95% CI: 0.58 – 0.60)	0.83	(95% CI: 0.82 – 0.85)	<0.001	0.58 (95% CI: 0.58 – 0.59)	0.80	(95% CI: 0.79 – 0.80) <0.001
BNF drug classes prescribed								
0	1.00	Reference	1.00	Reference	1.00	Reference	1.00	Reference
1-4	1.55	(95% CI: 1.50 – 1.61)	1.36	(95% CI: 1.32 – 1.41)	<0.001	1.78 (95% CI: 1.76 – 1.80)	1.69	(95% CI: 1.67 – 1.71) <0.001
5-9	3.21	(95% CI: 3.10 – 3.33)	2.09	(95% CI: 2.01 – 2.17)	<0.001	3.34 (95% CI: 3.31 – 3.37)	2.88	(95% CI: 2.85 – 2.91) <0.001
10-14	5.69	(95% CI: 5.48 – 5.92)	2.88	(95% CI: 2.76 – 3.00)	<0.001	5.72 (95% CI: 5.66 – 5.79)	4.48	(95% CI: 4.43 – 4.54) <0.001

15-19	9.28	(95% CI: 8.87 – 9.71)	4.03	(95% CI: 3.84 – 4.24)	<0.001	8.20	(95% CI: 8.09 – 8.31)	6.16	(95% CI: 6.07 – 6.25)	<0.001
≥20	11.28	(95% CI: 10.6 – 12.0)	4.95	(95% CI: 4.62 – 5.30)	<0.001	11.35	(95% CI: 11.2 – 11.6)	8.46	(95% CI: 8.29 – 8.63)	<0.001
Previous hospital admissions										
0	1.00	Reference	1.00	Reference		1.00	Reference	1.00	Reference	
1	1.69	(95% CI: 1.66 – 1.73)	1.04	(95% CI: 1.01 – 1.06)	0.013	1.61	(95% CI: 1.60 – 1.62)	1.02	(95% CI: 1.02 – 1.03)	<0.001
2	2.25	(95% CI: 2.18 – 2.33)	1.14	(95% CI: 1.09 – 1.19)	<0.001	2.09	(95% CI: 2.06 – 2.11)	1.07	(95% CI: 1.06 – 1.09)	<0.001
3	2.93	(95% CI: 2.80 – 3.05)	1.21	(95% CI: 1.14 – 1.29)	<0.001	2.52	(95% CI: 2.47 – 2.57)	1.10	(95% CI: 1.08 – 1.13)	<0.001
≥4	4.66	(95% CI: 4.50 – 4.83)	1.44	(95% CI: 1.35 – 1.53)	<0.001	2.71	(95% CI: 2.66 – 2.77)	1.16	(95% CI: 1.14 – 1.19)	<0.001
Past care home residence										
No	1.00	Reference	1.00	Reference		1.00	Reference	1.00	Reference	
Yes	7.52	(95% CI: 6.63 – 8.53)	1.66	(95% CI: 1.46 – 1.89)	<0.001	3.49	(95% CI: 3.33 – 3.66)	1.36	(95% CI: 1.29 – 1.42)	<0.001
NHS board of residence										
GG&C	1.00	Reference	1.00	Reference		1.00	Reference	1.00	Reference	
A&A	5.63	(95% CI: 5.44 – 5.83)	5.14	(95% CI: 4.96 – 5.32)	<0.001	1.00	(95% CI: 0.99 – 1.02)	0.98	(95% CI: 0.97 – 0.99)	<0.001
Borders	3.47	(95% CI: 3.27 – 3.68)	4.02	(95% CI: 3.80 – 4.27)	<0.001	0.77	(95% CI: 0.76 – 0.79)	0.87	(95% CI: 0.86 – 0.89)	<0.001
D&G	5.14	(95% CI: 4.90 – 5.39)	5.00	(95% CI: 4.76 – 5.24)	<0.001	0.88	(95% CI: 0.87 – 0.90)	0.91	(95% CI: 0.89 – 0.92)	<0.001
Fife	2.89	(95% CI: 2.77 – 3.01)	2.97	(95% CI: 2.85 – 3.10)	<0.001	0.94	(95% CI: 0.92 – 0.95)	0.97	(95% CI: 0.96 – 0.98)	<0.001
Forth Valley	0.53	(95% CI: 0.48 – 0.58)	0.61	(95% CI: 0.55 – 0.67)	<0.001	0.91	(95% CI: 0.90 – 0.93)	0.99	(95% CI: 0.98 – 1.01)	0.423
Grampian	5.34	(95% CI: 5.16 – 5.52)	5.64	(95% CI: 5.45 – 5.83)	<0.001	0.87	(95% CI: 0.87 – 0.88)	0.96	(95% CI: 0.95 – 0.97)	<0.001
Highland	3.36	(95% CI: 3.23 – 3.50)	3.30	(95% CI: 3.17 – 3.44)	<0.001	0.88	(95% CI: 0.87 – 0.89)	0.92	(95% CI: 0.91 – 0.93)	<0.001
Lanarkshire	3.59	(95% CI: 3.46 – 3.72)	3.61	(95% CI: 3.49 – 3.75)	<0.001	1.05	(95% CI: 1.04 – 1.06)	1.02	(95% CI: 1.01 – 1.03)	<0.001
Lothian	0.29	(95% CI: 0.27 – 0.31)	0.34	(95% CI: 0.32 – 0.37)	<0.001	0.92	(95% CI: 0.91 – 0.93)	1.06	(95% CI: 1.05 – 1.07)	<0.001
Orkney	5.87	(95% CI: 5.23 – 6.60)	5.10	(95% CI: 4.54 – 5.73)	<0.001	0.89	(95% CI: 0.84 – 0.94)	0.90	(95% CI: 0.85 – 0.95)	<0.001
Shetland	5.09	(95% CI: 4.47 – 5.81)	5.06	(95% CI: 4.44 – 5.77)	<0.001	0.88	(95% CI: 0.84 – 0.93)	0.90	(95% CI: 0.85 – 0.95)	<0.001
Tayside	1.27	(95% CI: 1.20 – 1.34)	1.21	(95% CI: 1.15 – 1.28)	<0.001	0.93	(95% CI: 0.92 – 0.94)	0.95	(95% CI: 0.94 – 0.96)	<0.001
WI	7.13	(95% CI: 6.60 – 7.71)	6.32	(95% CI: 5.85 – 6.83)	<0.001	1.04	(95% CI: 1.00 – 1.08)	0.99	(95% CI: 0.95 – 1.02)	0.445

GG&C = Greater Glasgow & Clyde; A&A = Ayrshire & Arran; D&G = Dumfries & Galloway; WI = Western Isles.

Table 6 (Supplemental): Urology cohort hazard ratios for ECOSS microbiological reports and PIS antibiotic prescriptions by all variables.

Variable	ECOSS reports			PIS prescriptions		
	Unadjusted	Adjusted		Unadjusted	Adjusted	
	HR (95% CI)	HR (95% CI)	*p*-value	HR (95% CI)	HR (95% CI)	*p*-value
Procedure						
No	1.00 Reference	1.00 Reference		1.00 Reference	1.00 Reference	
Yes	3.36 (95% CI: 2.87– 3.94)	3.40 (95% CI: 2.90 – 3.99)	<0.001	1.67 (95% CI: 1.59 – 1.76)	1.75 (95% CI: 1.66 – 1.84)	<0.001
Age group						
16-24	1.00 Reference	1.00 Reference		1.00 Reference	1.00 Reference	
25-34	1.35 (95% CI: 1.20 – 1.53)	1.30 (95% CI: 1.15 – 1.46)	<0.001	1.00 (95% CI: 0.98 – 1.01)	0.95 (95% CI: 0.94 – 0.97)	<0.001
35-44	2.23 (95% CI: 2.00 – 2.48)	1.95 (95% CI: 1.75 – 2.17)	<0.001	1.18 (95% CI: 1.16 – 1.19)	1.00 (95% CI: 0.98 – 1.01)	0.873
45-54	3.76 (95% CI: 3.39 – 4.17)	2.91 (95% CI: 2.62 – 3.23)	<0.001	1.48 (95% CI: 1.46 – 1.50)	1.06 (95% CI: 1.05 – 1.08)	<0.001
55-64	4.93 (95% CI: 4.46 – 5.46)	3.31 (95% CI: 2.99 – 3.67)	<0.001	1.69 (95% CI: 1.67 – 1.72)	1.05 (95% CI: 1.04 – 1.07)	<0.001
65-74	7.20 (95% CI: 6.51 – 7.97)	4.20 (95% CI: 3.79 – 4.65)	<0.001	1.98 (95% CI: 1.95 – 2.01)	1.06 (95% CI: 1.05 – 1.08)	<0.001
75-84	11.48 (95% CI: 10.4 – 12.7)	6.07 (95% CI: 5.48 – 6.73)	<0.001	2.33 (95% CI: 2.30 – 2.36)	1.13 (95% CI: 1.12 – 1.15)	<0.001
≥85	18.14 (95% CI: 16.3 – 20.2)	9.49 (95% CI: 8.49 – 10.6)	<0.001	2.68 (95% CI: 2.63 – 2.73)	1.29 (95% CI: 1.26 – 1.31)	<0.001
Charlson score						
0	1.00 Reference	1.00 Reference		1.00 Reference	1.00 Reference	
1-2	1.82 (95% CI: 1.76 – 1.87)	1.13 (95% CI: 1.10 – 1.17)	<0.001	1.42 (95% CI: 1.41 – 1.43)	1.04 (95% CI: 1.03 – 1.05)	<0.001
3-4	3.25 (95% CI: 3.11 – 3.39)	1.45 (95% CI: 1.39 – 1.52)	<0.001	1.80 (95% CI: 1.78 – 1.82)	1.08 (95% CI: 1.06 – 1.09)	<0.001
≥5	4.12 (95% CI: 3.87 – 4.38)	1.77 (95% CI: 1.66 – 1.90)	<0.001	1.93 (95% CI: 1.90 – 1.97)	1.13 (95% CI: 1.11 – 1.15)	<0.001
Unknown	0.65 (95% CI: 0.63 – 0.67)	0.92 (95% CI: 0.89 – 0.94)	<0.001	0.67 (95% CI: 0.66 – 0.67)	0.87 (95% CI: 0.87 – 0.88)	<0.001
BNF drug classes prescribed						
0	1.00 Reference	1.00 Reference		1.00 Reference	1.00 Reference	
1-4	1.66 (95% CI: 1.59 – 1.73)	1.21 (95% CI: 1.16 – 1.26)	<0.001	1.79 (95% CI: 1.78 – 1.81)	1.69 (95% CI: 1.68 – 1.71)	<0.001
5-9	3.26 (95% CI: 3.13 – 3.39)	1.67 (95% CI: 1.60 – 1.75)	<0.001	2.84 (95% CI: 2.82 – 2.87)	2.49 (95% CI: 2.47 – 2.52)	<0.001
10-14	5.03 (95% CI: 4.82 – 5.24)	2.19 (95% CI: 2.08 – 2.29)	<0.001	4.19 (95% CI: 4.15 – 4.23)	3.50 (95% CI: 3.46 – 3.53)	<0.001

15-19	7.07	(95% CI: 6.72 – 7.44)	2.79	(95% CI: 2.63 – 2.95)	<0.001	5.73	(95% CI: 5.67 – 5.80)	4.63	(95% CI: 4.57 – 4.69)	<0.001
≥20	8.99	(95% CI: 8.35 – 9.68)	3.42	(95% CI: 3.16 – 3.71)	<0.001	7.16	(95% CI: 7.04 – 7.29)	5.67	(95% CI: 5.57 – 5.78)	<0.001
Previous hospital admissions										
0	1.00	Reference	1.00	Reference		1.00	Reference	1.00	Reference	
1	1.66	(95% CI: 1.62 – 1.71)	1.04	(95% CI: 1.00 – 1.07)	0.026	1.46	(95% CI: 1.45 – 1.47)	1.00	(95% CI: 0.99 – 1.01)	0.970
2	2.15	(95% CI: 2.07 – 2.24)	1.07	(95% CI: 1.02 – 1.12)	0.002	1.72	(95% CI: 1.70 – 1.73)	1.01	(95% CI: 1.00 – 1.02)	0.007
3	2.72	(95% CI: 2.57 – 2.87)	1.18	(95% CI: 1.11 – 1.25)	<0.001	1.97	(95% CI: 1.95 – 2.00)	1.07	(95% CI: 1.06 – 1.09)	<0.001
≥4	3.90	(95% CI: 3.72 – 4.08)	1.54	(95% CI: 1.46 – 1.62)	<0.001	2.17	(95% CI: 2.14 – 2.20)	1.08	(95% CI: 1.07 – 1.10)	<0.001
Past care home residence										
No	1.00	Reference	1.00	Reference		1.00	Reference	1.00	Reference	
Yes	7.07	(95% CI: 6.57 – 7.60)	3.24	(95% CI: 3.01 – 3.49)	<0.001	2.43	(95% CI: 2.37 – 2.49)	1.40	(95% CI: 1.36 – 1.44)	<0.001
NHS board of residence										
GG&C	1.00	Reference	1.00	Reference		1.00	Reference	1.00	Reference	
A&A	0.80	(95% CI: 0.74 – 0.86)	3.07	(95% CI: 2.95 – 3.19)	<0.001	0.95	(95% CI: 0.94 – 0.96)	0.99	(95% CI: 0.98 – 1.00)	0.015
Borders	0.85	(95% CI: 0.81 – 0.90)	2.30	(95% CI: 2.14 – 2.48)	<0.001	0.97	(95% CI: 0.95 – 0.98)	1.01	(95% CI: 0.99 – 1.03)	0.363
D&G	0.58	(95% CI: 0.56 – 0.61)	2.37	(95% CI: 2.24 – 2.51)	<0.001	1.01	(95% CI: 0.99 – 1.02)	1.01	(95% CI: 0.99 – 1.02)	0.327
Fife	0.29	(95% CI: 0.27 – 0.31)	2.01	(95% CI: 1.93 – 2.10)	<0.001	0.87	(95% CI: 0.86 – 0.87)	0.97	(95% CI: 0.96 – 0.98)	<0.001
Forth Valley	0.94	(95% CI: 0.91 – 0.98)	0.98	(95% CI: 0.91 – 1.05)	0.595	0.91	(95% CI: 0.90 – 0.92)	0.98	(95% CI: 0.97 – 0.99)	0.002
Grampian	0.33	(95% CI: 0.32 – 0.34)	2.96	(95% CI: 2.85 – 3.08)	<0.001	0.93	(95% CI: 0.92 – 0.94)	1.01	(95% CI: 1.00 – 1.02)	0.011
Highland	0.61	(95% CI: 0.58 – 0.64)	1.81	(95% CI: 1.72 – 1.91)	<0.001	0.88	(95% CI: 0.87 – 0.89)	0.92	(95% CI: 0.91 – 0.93)	<0.001
Lanarkshire	0.79	(95% CI: 0.77 – 0.83)	2.41	(95% CI: 2.32 – 2.51)	<0.001	1.11	(95% CI: 1.10 – 1.12)	1.09	(95% CI: 1.09 – 1.10)	<0.001
Lothian	0.22	(95% CI: 0.21 – 0.23)	0.69	(95% CI: 0.65 – 0.73)	<0.001	1.00	(95% CI: 0.99 – 1.01)	1.06	(95% CI: 1.05 – 1.07)	<0.001
Orkney	1.14	(95% CI: 0.94 – 1.39)	3.28	(95% CI: 2.70 – 3.99)	<0.001	0.97	(95% CI: 0.91 – 1.03)	1.02	(95% CI: 0.96 – 1.09)	0.472
Shetland	0.89	(95% CI: 0.67 – 1.17)	2.88	(95% CI: 2.19 – 3.79)	<0.001	0.94	(95% CI: 0.87 – 1.01)	0.96	(95% CI: 0.89 – 1.04)	0.297
Tayside	0.32	(95% CI: 0.30 – 0.34)	1.09	(95% CI: 1.03 – 1.16)	0.004	0.88	(95% CI: 0.87 – 0.89)	1.00	(95% CI: 0.99 – 1.01)	0.606
WI	1.14	(95% CI: 1.01 – 1.28)	2.89	(95% CI: 2.56 – 3.26)	<0.001	1.03	(95% CI: 0.99 – 1.07)	0.96	(95% CI: 0.92 – 0.99)	0.023

GG&C = Greater Glasgow & Clyde; A&A = Ayrshire & Arran; D&G = Dumfries & Galloway; WI = Western Isles.