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Surveillance of bloodstream infections in intensive care units in England, May 2016–April 2017: epidemiology and ecology

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SUMMARY

Background: Bloodstream infections (BSIs) in patients in intensive care units (ICUs) are associated with increased morbidity, mortality and economic costs. Many BSIs are associated with central venous catheters (CVCs). The Infection in Critical Care Quality Improvement Programme (ICQIP) was established to initiate surveillance of BSIs in English ICUs.

Methods: A web-based data capture system was launched on 1st May 2016 to collect all positive blood cultures (PBCs), patient-days and CVC-days. National Health Service (NHS) trusts in England were invited to participate in the surveillance programme. Data were linked to the antimicrobial resistance dataset maintained by Public Health England and to mortality data.

Findings: Between 1st May 2016 and 30th April 2017, 84 ICUs (72 adult ICUs, seven paediatric ICUs and five neonatal ICUs) based in 57 of 147 NHS trusts provided data. In total, 1474 PBCs were reported, with coagulase-negative staphylococci, *Escherichia coli*, *Staphylococcus aureus* and *Enterococcus faecium* being the most commonly reported organisms. The rates of BSI and ICU-associated CVC-BSI were 5.7, 1.5 and 1.3 per 1000 bed-days and 2.3, 1.0 and 1.5 per 1000 ICU-CVC-days in adult, paediatric and neonatal ICUs, respectively. There was wide variation in BSI and CVC-BSI rates within ICU types, particularly in adult ICUs (0–44.0 per 1000 bed-days and 0–18.3 per 1000 ICU-CVC-days).

Conclusions: While the overall rates of ICU-associated CVC-BSIs were lower than 2.5 per 1000 ICU-CVC-days across all age ranges, large differences were observed between ICUs, highlighting the importance of a national standardized surveillance system to identify

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opportunities for improvement. Data linkage provided clinically important information on resistance patterns and patient outcomes at no extra cost to participating trusts.

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Introduction

Patients in intensive care units (ICUs) in England are disproportionately affected by healthcare-associated infections (HCAs); in a 2011 national point prevalence survey, patients in adult ICUs accounted for 3% of the hospital population but 9% of all HCAs [1]. Device usage was higher among patients in ICUs than the general hospitalized population, particularly central venous catheter (CVC) usage (59.3% vs 5.9%). CVCs are a necessary supportive technology for many critically ill patients, but they also create a potential portal of entry for pathogens that may cause bloodstream infections (BSIs). CVC-BSIs are associated with increased risk of death (25%) and cost of care [2,3]. However, considerable reductions in CVC-BSIs are possible [4–7], exemplified by the Keystone-Michigan project in which five evidence-based infection control procedures combined with a programme to optimize safety culture were associated with a reduction in the mean rate of CVC-BSIs from 7.7 to 1.4 infections per 1000 CVC-days [6].

In England in 2008, the National Health Service (NHS) Next Stage Review announced that the National Patient Safety Agency would run an initiative to prevent CVC-BSIs using the Keystone-Michigan project as a model. The Matching Michigan project [8] was funded by the UK Department of Health and undertaken in 196 adult and 19 paediatric ICUs across England. This 2-year four-cluster stepped-wedge interventional non-randomized study encompassed both evidence-based technical interventions and non-technical interventions to encourage positive behavioural and systems change. It reported reductions in the mean rate of CVC-BSIs for both adult (3.7–1.48 per 1000 CVC-days) and paediatric (5.65–2.89 per 1000 CVC-days) ICUs. However, among the adult ICUs, each cluster that joined the study had a similar pre-entry CVC-BSI rate to post-interventional rates of clusters already in the study. Moreover, CVC-BSIs not characterized as ICU-associated (i.e. among patients hospitalized in the ICU for <2 nights, and therefore assumed to have been acquired before ICU admission) declined at a similar rate as ICU-associated BSIs, indicating a systems-wide cause for improvement.

Conducted in parallel with the Matching Michigan project, an independent ethnographic study, 'What counts' [9,10], undertaken in 19 ICUs, provided unique insights into the way in which the patient safety programme actually operated in these ICUs. Although infection control practices and staff focus were largely good, the non-technical interventions were poorly adopted; clinical staff expressed concerns that the definitions for CVC-BSIs did not fairly represent local circumstances and case mix.

A key conclusion from the Matching Michigan study was the need to establish a permanent, standardized national infection surveillance and reporting system in ICUs in England, with strong clinical ownership required for sustainable success [8]. Consequently, a multi-professional collaboration of organizations representing adult, paediatric and neonatal intensive

care medicine, microbiology and infection control was formed in 2011, known as the 'Infection in Critical Care Quality Improvement Programme' (ICCQIP). To determine clinical engagement and priorities for the improvement programme, a national survey was distributed to staff in all ICUs through stakeholder organizations in December 2012. In total, 763 replies were received; 80% were clinicians, 8% were critical care nurses and 4.7% were microbiologists, 94% of whom supported establishing a national surveillance programme [11]. Respondents prioritized CVC-associated BSIs and multi-resistant infections.

Unlike Keystone-Michigan or Matching Michigan, the ICCQIP surveillance programme aimed to collect individual patient-level data with definitions of BSIs, CVC-associated and CVC-related infections determined via systematic analysis of the raw data (Table S1, see online supplementary material) rather than reported pre-applied via clinician judgement. Standardized objectively verifiable definitions were developed from existing international guidance to permit comparisons across geographies. Furthermore, collecting patient-level data allowed for data linkage to established datasets on antimicrobial resistance (AMR) and patient outcomes, reducing the burden of data collection on ICU staff while enhancing the data to include important clinical information that was not previously available.

In 2013, a paper-based pilot surveillance tool was designed, and in 2014, an online data capture system was developed. In May 2016, a sentinel surveillance programme in England assessing CVC-BSIs was rolled out and then opened to all ICUs in the country in November 2016. The data on PBCs and BSIs (all, ICU-associated and ICU-CVC) collected and linked over the first year of this surveillance programme are presented here, providing a description of the current status of BSIs in ICUs along with their AMR distribution.

Methods

Site selection

Sentinel sites were self-selected following distribution of an invitation in November 2015 through the collaborating organizations associated with ICCQIP. In November 2016, the invitation to participate was extended to all acute NHS trusts (hospitals under the same management) in England.

Data collection

Patient-level data for each PBC episode from participating sites were collected. An episode was defined as a 7-day period; new PBCs yielding the same pathogens within 7 days of the initial specimen were considered to be duplicates. Up to four organisms could be entered per episode if these were cultured from the same blood sample set. Multiple blood culture sets

taken per patient on the same day with different culture results were reported separately.

Data were collected on patient demographics, symptoms present at the time of blood culture, repeat PBCs for patients with a likely skin commensal, presence of CVCs and microbiological evidence linking the CVC to the PBC, usage of antimicrobial therapy and potential alternative sources of infection. These data allowed standardized algorithms to define whether a PBC was considered to be indicative of a BSI, if the BSI was ICU-associated and if the BSI was linked to a CVC (see online supplementary material for definitions).

ICUs were also asked to enter denominator data each month, detailing the total number of occupied overnight bed-days, total number of occupied overnight bed-days for patients in the ICU for >2 nights, CVC-days for patients in the ICU for >2 nights and total number of blood culture sets taken.

Data linkage

Data linkage allows for enhancement of the surveillance dataset, without incurring additional costs to participating NHS trust ICUs or increased burden of data capture.

Patient-level data were linked to records in two other datasets: Public Health England's (PHE) Second Generation Surveillance System (SGSS) AMR dataset [12]; and the NHS Spine [13], a central repository of patient information, containing data on patient mortality.

SGSS AMR data were extracted on 2nd December 2019, covering 1st January 2016 to 27th September 2017, and were linked to the ICCQIP surveillance data using various patient identifiers and the bacterial species. SGSS AMR data were retained if the specimen date from the AMR dataset was ± 6 days from the ICU specimen date; this was curtailed if the AMR specimen date preceded ICU admission.

Data were linked to NHS Spine via the demographic batch service [14] on 29th September 2017. This was to obtain mortality status and date of death (if deceased). Case fatality rates (CFRs) were calculated for 30-day all-cause mortality following a PBC. As the length of a PBC episode was 7 days, a single patient may have had multiple episodes within 30 days of death. Only the PBC closest to the date of death (within the preceding 30 days) was retained in the CFR calculation. Furthermore, this de-duplication was applied to patients without a death date but with more than one episode within 30 days of their final specimen date, thus ensuring standardized rules and processes were set for obtaining numerators and denominators.

Data analyses

Analyses were performed in Stata 15.1 [15]. Data for all PBCs and denominator values were extracted from the ICCQIP data capture system on 7th July 2017. Imputation for missing denominators was completed for ICUs with some denominator data (see online supplementary material).

Due to the low numbers of paediatric and neonatal reported PBCs, analyses of reported organisms and AMR were performed on the full dataset, and CFRs were calculated for adult ICUs and paediatric and neonatal ICUs grouped together. However, counts and rates of various infection metrics were calculated overall and by ICU type (adult, paediatric and neonatal).

Table 1

Recruitment of National Health Service (NHS) acute trust intensive care units (ICUs) to the Infection in Critical Care Quality Improvement Programme sentinel surveillance programme: May 2016–April 2017

| | NHS acute trusts | ICUs | | | |
|--|------------------|------------|-------------------------|--------------------------------|------------------------------|
| | | Total ICUs | Adult [16] ^a | Paediatric [17] ^{a,b} | Neonatal [18] ^{a,b} |
| Total number in England | 147 | 426 | 236 | 24 | 165 |
| Total who have provided at least one ICU for entry on to the DCS | 122 | 243 | 202 | 22 | 19 |
| Total with a LA signed up to the system | 98 | 194 | 164 | 17 | 13 |
| Total with data entered on to the system May 2016–April 2017 | 57 | 84 | 72 | 7 | 5 |

DCS, data capture system; LA, Local Administrator.

^a Numbers have been calculated from the list of named participating sites from English NHS acute trusts. Independent sector sites within England have been excluded, as have sites from Northern Ireland, Scotland and Wales.

^b Two units have been excluded from the paediatric list provided that are from NHS acute trusts in England; one is an adult ICU with two paediatric beds (Hull Royal Infirmary adult ICU) which has been included in the adult ICU total, and the second is the neonatal ICU from Great Ormond Street, which has been added to the neonatal ICU total.

Results

Enrolment

As of July 2017, 122 of 147 NHS acute trusts had responded to the invitation to participate in the study, with local administrators registered for 98 trusts, representing 194 ICUs (45.5% of all ICUs in the country; adult: 69.5%, paediatric: 70.8%, neonatal: 7.8%). Of these, 57 trusts (84 units) participated in the surveillance programme in its inaugural year [72 adult ICUs (85.7%), seven paediatric ICUs (8.3%) and five neonatal ICUs (6.0%)] (Table 1).

Counts and rates of infection

During the first 12 months of the surveillance programme (1st May 2016–30th April 2017), 1474 PBCs were reported: 90.9% ($N=1340$) from adult ICUs, 4.9% ($N=72$) from paediatric ICUs and 4.2% ($N=62$) from neonatal ICUs. Data from 12 ICUs were excluded from the rate calculations due to missing denominator data (10 adult ICUs and two neonatal ICUs), leaving 1417 PBCs (96.1% of those entered) from a reported 19,089 blood culture sets taken.

From adult ICUs, 56% of PBCs met the criteria to be defined as a BSI; this was lower for paediatric (41.7%) and neonatal (25.8%) ICUs, giving rates of BSIs per 1000 patient-days of 5.7, 1.5 and 1.0, respectively (Table II). Individual ICUs varied widely in calculated BSI rates (adult ICUs: 0.0–44.0 BSIs per 1000 patient-days; paediatric ICUs: 0.0–8.8 BSIs per 1000

Table II

Positive blood cultures (PBCs), bloodstream infections (BSIs), intensive care unit (ICU)-associated BSIs and central venous catheter (CVC)-BSIs by ICU type: May 2016–April 2017

| | ICU type (age category) | | |
|--|-------------------------|------------|----------|
| | Adult | Paediatric | Neonatal |
| Total PBCs ^a | 1292 | 72 | 53 |
| Total blood culture sets taken | 16601 | 1365 | 1123 |
| Total BSIs | 724 | 30 | 16 |
| Occupied overnight bed-days | 126011 | 20320 | 16189 |
| Rate of blood culture sets taken per 1000 occupied overnight bed-days | 131.7 | 67.2 | 69.4 |
| Rate of BSIs per 1000 occupied overnight bed-days | 5.7 | 1.5 | 1.3 |
| ICU-associated BSIs | 433 | 19 | 11 |
| Occupied overnight bed-days, restricted to include patients in ICU >2 nights | 88411 | 8958 | 14995 |
| Rate of ICU-associated BSIs per 1000 occupied overnight ICU-bed-days | 4.9 | 2.1 | 0.7 |
| ICU-associated CVC-BSIs | 124 | 5 | 5 |
| ICU-CVC-days | 53913 | 5002 | 3304 |
| Rate of ICU-associated CVC-BSIs, per 1000 ICU-CVC-days | 2.3 | 1.0 | 1.5 |
| CVC utilization | 61.0% | 55.8% | 22.0% |

^a Number of PBCs is lower in Table II than the overall total PBCs reported, as these data are used in rates. Numerator data for ICUs that did not provide any denominator data have been excluded from this analysis.

patient-days, neonatal ICUs: 0.9–1.1 BSIs per 1000 patient-days).

The majority of BSIs were ICU-associated, defined as a BSI occurring >2 days (or >48 h if specimen and admission times were provided) after ICU admission, with rates per ICU type of 4.9, 2.1 and 0.7 per 1000 ICU patient-days for adult, paediatric and neonatal ICUs, respectively. Of the ICU-associated BSIs, the percentage which were defined as CVC-BSIs varied by type of ICU, with rates of 2.3, 1.0 and 1.5 ICU-associated CVC-BSIs per 1000 ICU-CVC-days among adult, paediatric and neonatal ICUs, respectively (Table II).

The overall blood culture sampling rate varied by ICU type, from 67.2 per 1000 patient-days in paediatric ICUs to 131.7 in adult ICUs (Table II). However, there was large variation in blood culture sampling rates within ICU types, particularly amongst adult ICUs, with a range of 0–1142 per 1000 patient-days (Table III).

Reported organisms

Among adults, 48% ($N=644/1340$) of PBCs yielded skin commensals; this was higher amongst paediatric and neonatal PBCs (61% and 57%, respectively). However, <3% of skin commensal PBCs could be defined as BSIs, largely because the majority (81.9%) of these PBCs were missing the required repeat blood sample taken within 48 h of the first culture set (range 45.5–91.4% missing by ICU type; Table S4, see online supplementary material). Polymicrobial infections (multiple organisms from the same culture or from multiple blood culture

sets taken on the same calendar day) accounted for 12.1% ($N=178$) of all PBCs.

From 1474 PBC episodes, 1635 organisms were reported, 78% of which ($N=1270$) were attributable to 10 species (Figure 1a). The most frequently reported organisms in ICUs were coagulase-negative staphylococci (CoNS) (40.1%), *Escherichia coli* (9.3%) and *Staphylococcus aureus* (6.1%). PBC episodes of *Enterococcus faecium* accounted for 5% of all cultures from ICUs. However, restricting the analysis to ICU-associated BSI reduced CoNS to 8.9%, lower than *E. coli* (11.6%) and *E. faecium* (11.5%).

Antimicrobial resistance

PBC episodes were linked to PHE's SGSS AMR dataset. For the top 10 organisms, the percentage of episodes linked ranged from 68% to 83% (Table III, bacterial organisms only).

Just over one in five linked *E. coli* isolates were found to be resistant to piperacillin/tazobactam (21.0%), ciprofloxacin (22.0%) and third-generation cephalosporins (20.0%). The majority of linked *E. coli* were resistant to amoxicillin/clavulanate and ampicillin/amoxicillin (55.6% and 71.3%, respectively).

Of linked *Klebsiella pneumoniae* isolates, 15.2% were resistant to third-generation cephalosporins and 19.6% were resistant to piperacillin/tazobactam. Resistance to ertapenem or meropenem was seen in 4.8% and 1.8% of linked *K. pneumoniae*, respectively. Among linked *Klebsiella oxytoca* isolates, 13.3% were resistant to piperacillin/tazobactam.

Of linked *Enterobacter cloacae* isolates, 53.3% were resistant to third-generation cephalosporins, 51.9% to piperacillin/tazobactam, 14.8% to ertapenem, 12.9% to gentamicin, 11.8% to tobramycin and 10.0% to ciprofloxacin.

Among linked *Pseudomonas aeruginosa*, resistance to carbapenems was high [meropenem 13.5% and imipenem 27.3%, although the number of organisms tested against the latter was small ($N=11$)]. Furthermore, 16.2% were resistant to ciprofloxacin.

Among the Gram-positive bacteria most frequently reported from the ICUs, 7.6% of linked *S. aureus* were methicillin-resistant and 22% of linked *E. faecium* were glycopeptide-resistant.

All-cause 30-day mortality

All-cause 30-day mortality was assessed through linkage of the ICCQIP PBC data with the NHS Spine dataset. Of 1474 PBCs, 178 (12.1%) patient episodes were excluded from this analysis because they could not be linked to the NHS Spine dataset (i.e. missing/inaccurate NHS numbers or dates of birth), were defined as post-mortem (ICU specimen date >2 days after returned date of death) or multiple episodes from the same patient occurred within the 30 days preceding death/final specimen date. Among the 1296 matched cases, 291 died within 30 days of the final PBC, giving an overall 30-day all-cause CFR of 22.5% [95% confidence interval (CI) 20.2–24.8%, Table IV]. There were differences by ICU type, with a higher CFR found amongst adult ICUs (23.8%, 95% CI 21.4–26.4%) compared with paediatric/neonatal ICUs (9.1%, 95% CI 4.6–15.7%).

Table III

Antimicrobial resistance (AMR) among the most commonly reported bacterial organisms circulating in intensive care units (ICUs) in England: May 2016–April 2017

| Organism name | <i>E. coli</i> | | <i>K. pneumoniae</i> | | <i>K. oxytoca</i> | | <i>E. cloacae</i> | | <i>P. aeruginosa</i> | | <i>E. faecium</i> | | <i>E. faecalis</i> | | <i>S. aureus</i> | | CoNS | |
|--|--------------------|------|----------------------|-------|-------------------|-------|-------------------|------|----------------------|------|-------------------|-------------------|--------------------|-----|------------------|------|--------------------|------|
| | T | % R | T | % R | T | % R | T | % R | T | % R | T | % R | T | % R | T | % R | T | % R |
| Match with AMR dataset | (N=126/152, 82.9%) | | (N=55/69, 79.7%) | | (N=16/20, 80.0%) | | (N=31/38, 81.6%) | | (N=37/53, 69.8%) | | (N=62/81, 76.5%) | | (N=21/31, 67.7%) | | (N=79/99, 79.8%) | | (N=478/670, 71.3%) | |
| Amoxicillin/clavulanate | 124 | 55.6 | 54 | 35.2 | 16 | 25.0 | - | - | - | - | - | - | - | - | - | - | - | - |
| Ampicillin/amoxicillin | 122 | 71.3 | 54 | 100.0 | 15 | 100.0 | - | - | - | - | 59 | 96.6 ^a | 18 | 0.0 | - | - | - | - |
| Piperacillin/tazobactam | 119 | 21.0 | 51 | 19.6 | 15 | 13.3 | 27 | 51.9 | 36 | 5.6 | - | - | - | - | - | - | - | - |
| Gentamicin | 124 | 9.7 | 52 | 3.8 | 16 | 0.0 | 31 | 12.9 | 37 | 0.0 | - | - | - | - | 78 | 2.6 | 440 | 53.9 |
| Ciprofloxacin | 123 | 22.0 | 53 | 9.4 | 16 | 0.0 | 30 | 10.0 | 37 | 16.2 | - | - | - | - | 66 | 12.1 | 380 | 58.9 |
| Third-generation cephalosporins ^b | 108 | 19.4 | 50 | 16.0 | 14 | 0.0 | 31 | 54.8 | - | - | - | - | - | - | - | - | - | - |
| Cefotaxime | 54 ^c | 25.9 | 27 ^c | 14.8 | 7 ^c | 0.0 | 17 ^c | 64.7 | - | - | - | - | - | - | - | - | - | - |
| Ceftazidime | 105 | 18.1 | 46 | 13.0 | 13 | 0.0 | 30 | 56.7 | 36 | 5.6 | - | - | - | - | - | - | - | - |
| Imipenem | - | - | - | - | - | - | - | - | 11 | 27.3 | - | - | - | - | - | - | - | - |
| Meropenem | 123 | 0.0 | 55 | 1.8 | 14 | 0.0 | 31 | 0.0 | 37 | 13.5 | - | - | - | - | - | - | - | - |
| Ertapenem | 90 | 1.1 | 42 | 4.8 | 13 | 0.0 | 27 | 14.8 | - | - | - | - | - | - | - | - | - | - |
| Amikacin | 86 ^c | 0.0 | 38 ^c | 0.0 | 9 | 0.0 | 25 | 0.0 | 26 | 0.0 | - | - | - | - | - | - | - | - |
| Tobramycin | 39 ^c | 17.9 | 21 ^c | 4.8 | 7 ^c | 0.0 | 17 ^c | 11.8 | 14 ^c | 0.0 | - | - | - | - | - | - | - | - |
| Colistin | 16 ^c | 0.0 | 6 ^c | 0.0 | 2 ^c | 0.0 | - | - | 10 ^c | 0.0 | - | - | - | - | - | - | - | - |
| Glycopeptides ^d | - | - | - | - | - | - | - | - | - | - | - | - | 21 | 0.0 | 52 ^c | 0.0 | 293 ^c | 13.7 |
| Vancomycin | - | - | - | - | - | - | - | - | - | - | 60 | 21.7 | 21 | 0.0 | 45 ^c | 0.0 | 237 ^c | 0.8 |
| Teicoplanin | - | - | - | - | - | - | - | - | - | - | 55 | 23.6 | 17 | 0.0 | 48 ^c | 0.0 | 214 ^c | 17.8 |
| Erythromycin | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 72 | 23.6 | 453 | 71.3 |
| Linezolid | - | - | - | - | - | - | - | - | - | - | 59 | 0.0 | 20 | 5.0 | 72 | 0.0 | 377 | 0.8 |
| Rifampicin | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 75 | 1.3 | 414 | 17.1 |
| Mupirocin | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 61 | 0.0 | 297 ^c | 33.0 |
| Meticillin ^e | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 66 ^f | 7.6 | 410 | 75.1 |
| Fusidic acid | - | - | - | - | - | - | - | - | - | - | - | - | - | - | 76 | 10.5 | 449 | 65.7 |

T, tested; R, resistant; *E. coli*, *Escherichia coli*; *K. pneumoniae*, *Klebsiella pneumoniae*; *K. oxytoca*, *Klebsiella oxytoca*; *E. cloacae*, *Enterobacter cloacae*; *P. aeruginosa*, *Pseudomonas aeruginosa*; *E. faecium*, *Enterococcus faecium*; *E. faecalis*, *Enterococcus faecalis*; *S. aureus*, *Staphylococcus aureus*; CoNS, coagulase-negative staphylococci.

^a Intrinsically resistant.

^b Cefotaxime or ceftazidime.

^c Less than 75% of the data linked to Public Health England's Second Generation Surveillance System tested for this antimicrobial, so there may have been selective testing.

^d Vancomycin or teicoplanin.

^e Meticillin, oxacillin, cloxacillin or ceftazidime.

^f Sixty-one meticillin-susceptible *Staphylococcus aureus* bloodstream infections of the 66 *S. aureus* bloodstream infections, of which 16.7% were resistant to erythromycin and 10.3% were resistant to fusidic acid (0.0% resistance to all other relevant antimicrobials reported in Table III).

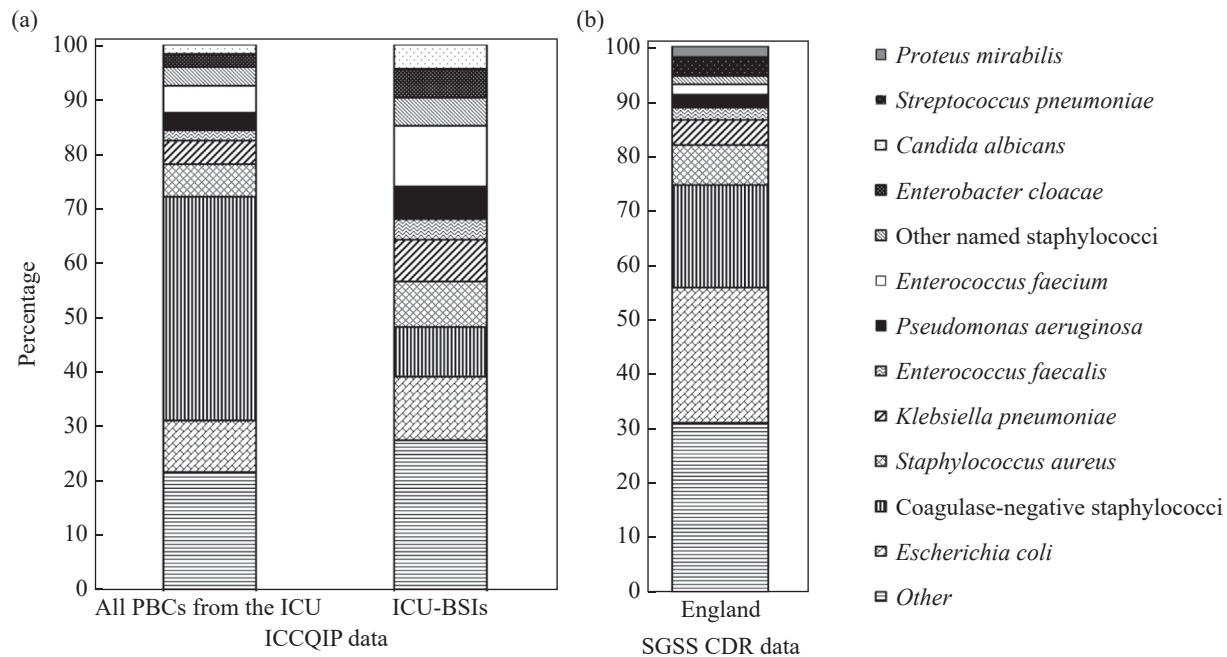


Figure 1. Top ten bacteraemia-/fungaemia-causing organisms in (a) intensive care units (ICUs) participating in the Infection in Critical Care Quality Improvement Programme (ICCQIP) surveillance programme and (b) England [Public Health England's Second Generation Surveillance System (SGSS) communicable disease reporting (CDR) 2016 data] [21]. The SGSS CDR data comprise all positive blood cultures (PBCs) in England, including the positive blood cultures reported to ICCQIP. BSIs, bloodstream infections.

Discussion

Epidemiology

ICCQIP was established following the Matching Michigan project to provide ICUs with locally owned, nationally benchmarked data on CVC-BSIs. CVC-BSI rates in adult ICUs were higher than recorded at the end of the Matching Michigan study

Table IV

Case fatality rate (CFR) of patients with a positive blood culture in intensive care units (ICUs)

| ICU type (age category) | Reports ^a | Linked reports ^b | Deaths ^c | CFR ^d | Lower 95% CI | Upper 95% CI |
|-------------------------------|----------------------|--------------------------------|---------------------|------------------|-----------------|-----------------|
| Adult | 1340 | 1175 | 280 | 23.8 | 21.4 | 26.4 |
| Paediatric/ neonatal | 134 | 121 | 11 | 9.1 | 4.6 | 15.7 |

CI, confidence interval.

^a Represents reports of positive blood cultures made to the Infection in Critical Care Quality Improvement Programme for infections detected 1 May 2016–30 April 2017.

^b Excludes reports which failed to link to NHS Spine, reports where the date of death was ≥ 2 days before the specimen date and where there were more than one PBC within 30 days of final ICU specimen date.

^c Mortality information obtained by linking reports with a complete NHS number and date of birth to NHS Spine.

^d Calculated as the number of deaths divided by the number of reports with complete NHS number, multiplied by 100. The numerator and denominator may count the same patient more than once as the rate is based on reports rather than patients.

(2.3 vs 1.5 per 1000 ICU-CVC-days, respectively), and lower in paediatric ICUs (1.0 vs 2.9 per 1000 ICU-CVC-days) [8], implying that the reductions seen in the Matching Michigan project were not sustained in adults. However, methodological differences between the ICCQIP surveillance programme and the Matching Michigan study may affect the direct comparability of these data. In the latter, clinicians determined whether a BSI episode was catheter-associated (CABSI) or catheter-related (CRBSI) (Table S3, see online supplementary material), with the overall burden of CVC-BSI calculated as the sum of CABSI and CRBSI. However, as clinicians determined whether an episode met either of these definitions, variability in applying the definitions may have occurred. In the ICCQIP surveillance programme, standardized definitions are applied to patient-level data and may account for the higher rates observed amongst adult ICUs. Differences noted between the paediatric ICUs may be due to the lower participation of paediatric ICUs in the ICCQIP surveillance programme than in the Matching Michigan project, with low numbers of paediatric PBCs reported overall.

While the overall crude rates of BSI and ICU-CVC-BSI identified in ICUs are under 6.0 per 1000 bed-days and 2.5 per 1000 ICU-CVC-days, the range in values for individual ICUs varied greatly. One of the key strengths of this surveillance programme is that black and white algorithms for the defined infection types are applied to reported raw data; therefore, these observed differences are not due to differences in interpretation by participating ICUs. However, they could represent a denominator effect from small numbers, inexperience with reporting in the early stages of the programme, between-ICU differences in case mix and patient susceptibility, a true difference in infection control practices, or variation in blood culture sampling rates. A large variation in sampling rates was reported by English ICUs. This has been identified

previously in the Matching Michigan project and among ICUs in Germany [19]. While low sampling rates might underestimate the number of BSIs, and higher rates might increase false-positive results and waste resources, the optimum culturing rate is not known. A population-based study suggests that a plateau may be reached for a culture rate >5550 per 100,000 population [20], but these data do not relate specifically to critically ill patients. However, the variation between ICUs in sampling and CVC-BSI rates highlights the potential of this surveillance programme for raising awareness and setting a standardized benchmark. Future plans include linking ICCQIP data to current ICU case-mix programmes to provide risk-adjusted infection rates for all ICU patients in England.

Ecology

The top 10 organisms identified from PBCs from ICUs differed from those from the general population [SGSS communicable disease reporting (CDR) dataset [21]] in composition, rank and percentage (Figure 1a vs 1b). In the national SGSS CDR dataset, *E. coli* was the most frequently identified organism (24.7% vs 9.3% among ICU specimens). In addition, nationally, a lower proportion of PBCs are due to CoNS than in ICUs; while all should be reported to SGSS, some suppression may be occurring, accounting for this difference. Furthermore, within ICUs, CoNS accounted for a lower proportion of ICU-associated BSIs than all PBCs, because many did not meet the BSI definition for skin commensals. Alternative explanations include contamination of blood culture sets (a target for quality improvement), BSIs being misclassified due to the need for a repeat PBC within 48 h when it may not be standard clinical practice to collect another blood culture before the previous results were known, or growth suppression from antimicrobials which may cause subsequent negative blood cultures (if they were taken).

E. faecium accounted for <2% of all of England's bacteraemia/fungaemia in 2016, compared with 5% of PBCs in ICUs and 11% of ICU-associated BSIs. Furthermore, the ratio between *Enterococcus faecalis* and *E. faecium* differs between England as a whole and ICUs, with *E. faecalis* the predominant enterococcal species in England. However, in ICUs (total PBCs or ICU-BSI) there were >2.5 times the number of reported *E. faecium* compared with *E. faecalis*; this is an important finding as *E. faecium* is generally more resistant to antibiotics than *E. faecalis*, especially β -lactam antibiotics [22] (intrinsically resistant) and glycopeptides [23]. Of note, the SGSS comparison is of previously published data and so will include the ICU PBCs. However, as the number of ICU PBCs is only a small proportion of all PBCs in the SGSS CDR dataset, this should not affect the comparison with national-level data.

The prevalence rates of different organisms of reported PBCs by ICU type were assessed; while differences were found, the numbers of paediatric and neonatal PBCs were too small once stratified by organism (Table S4, see online supplementary material), so no conclusions can be made at this time.

Antimicrobial resistance within English ICUs

Not only are the species which cause bacteraemia/fungaemia in English ICUs different from the population as a whole, the data linkage with the SGSS AMR dataset has shown that the Gram-negative causative organisms in ICUs are also generally

more resistant to antimicrobials. For example, the *E. coli* PBCs in ICUs were twice as resistant to piperacillin/tazobactam and third-generation cephalosporins than among those reported to the mandatory national surveillance of *E. coli* bacteraemia programme [24] (21.0% vs 10.2% and 20.0% vs 10.4%, respectively) and 1.3 times more resistant to tobramycin and amoxicillin/clavulanate compared with *E. coli* bacteraemias reported to PHE's SGSS AMR dataset [25].

AMR among *K. pneumoniae* PBCs was between 1.5 and 4.6 times higher in ICU patients than among the general population [26] (piperacillin/tazobactam 19.6% vs 13.3%; ceftazidime 14.8% vs 10.1%; cefotaxime 13.0% vs 10.2%; meropenem 1.8% vs 0.5%; ertapenem 4.8% vs 1.0%). In addition, a two-fold difference in the percentage of resistance against ciprofloxacin (16.2% vs 7.2%), meropenem (13.5% vs 5.5%) and imipenem (27.3% vs 11.2%) was identified among ICU patient episodes of *P. aeruginosa* than nationally [27]. Furthermore, the percentage of resistant *E. cloacae* from ICUs was 1.6–3.3 times higher than among *Enterobacter* spp. bacteraemia reported in England for gentamicin, ciprofloxacin, ceftazidime, cefotaxime, ertapenem, tobramycin and piperacillin/tazobactam [28].

Data linkage with PHE's SGSS AMR dataset has provided a wealth of data that would otherwise be unknown nationally in the ICU setting. Clinically, this has repercussions when clinicians often have to treat their patients empirically, before organism identification and antimicrobial susceptibility results are available. The generally higher levels of AMR are likely to be a consequence of higher antimicrobial usage in ICUs than in other hospital specialties [29], contributing to antibiotic-resistant selection pressure directly among ICU patients, and indirectly among ICU staff and the environment. This highlights the need for intensivists and pharmacists to consider antibiotic susceptibility data from their ICU patients rather than relying on the wider trends in the overall patient population. It also emphasizes the need for antimicrobial stewardship to minimize selection pressures.

Mortality

The overall CFR was 22.5% and the CFR among ICU-associated BSIs was 25.7%. Mortality among adult patients with ICU-associated BSIs in an English ICU from 2009 to 2013 was reported at >30% [30], and the result was similarly high among patients with an ICU-BSI from the BASIC study [31] with data from 132 ICUs in 26 countries. However, as the causative organisms for all BSIs in England have changed over time, from predominantly *S. aureus* to a greater percentage caused by *E. coli* [32], and the relative CFRs are higher in meticillin-resistant *S. aureus* compared with *E. coli* [33], the usefulness of comparing ICU data with these prior studies is limited.

In conclusion, the ICCQIP programme has successfully attracted a large proportion of ICUs to participate, allowing trends to be measured and issues to be identified and tackled, ultimately working towards reducing ICU-associated BSIs. Data linkage with AMR and patient outcome datasets has allowed for enhanced surveillance without additional cost or burden to participating NHS ICUs, providing clinically important data that would otherwise not be possible to look at nationally. Initial data from this surveillance highlight the differences between infections occurring in ICUs and the wider patient population, especially with regard to species and antibiotic resistance distributions. With the surveillance scheme now launched

nationally, work on barriers and facilitators to participation will be assessed in order to increase the number of ICUs in England providing data, as well as identifying other levers to help aid in participation, particularly in neonatal ICUs for which there is currently low representation.

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Conflict of interest statement

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhin.2020.05.010>.

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