Risk-adjusted monitoring of blood-stream infection in paediatric intensive care: a data linkage study

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Purpose

National monitoring of variation in the quality of infection control in paediatric intensive care units (PICUs) requires comparisons of risk-adjusted rates. To inform the development of a national monitoring system, we evaluated the effects of risk-adjustment and outcome definition on comparisons of blood-stream infection (BSI) rates in PICU, using linkage of risk-factor data captured by national audit (PICANet) with laboratory records of BSI.

Methods

Admission data for two children's hospitals 2003-2010 were extracted from PICANet and linked using multiple identifiers with laboratory BSI records. We calculated trends of PICU-acquired BSI, defined as BSI occurring between >=2 days after admission until <=2 days following discharge. In one PICU, we compared rates of all PICU-acquired BSI with clinically significant PICU-acquired BSI submitted to the national surveillance system.

Results

1428 (6.8%) of 20,924 admissions were linked to 1761 PICU-acquired BSI episodes. The crude incidence rate-ratio for PICU-acquired BSI between PICUs was 1.15 (95% confidence interval (CI) 1.05-1.26) but increased to 1.26 (1.14-1.39) after risk-adjustment. Rates of PICU-acquired BSI were 13.44 (95% CI 12.60-14.28) per 1000 bed-days at PICU 1 and 18.05 (95% CI 16.80-19.32) at PICU 2. Of PICU-acquired BSI at PICU 2, 41% was classified as clinically significant. Rates of PICU-acquired BSI decreased by 10% per year between 2003-2010 for skin organisms and 8% for non-skin organisms.

Conclusions

Risk-adjustment and standardisation of outcome measures are essential for fair comparisons of BSI rates between PICUs. Linkage of risk-factor data and BSI surveillance is feasible and could allow national risk-adjusted monitoring.

Key words: blood-stream infection, surveillance, data linkage, paediatric intensive care, risk-adjustment, bacteraemia

INTRODUCTION

Healthcare-associated infection (HAI) is an important cause of adverse clinical outcome and cost to the UK National Health Service (NHS), and paediatric intensive care units (PICUs) have one of the highest reported rates of nosocomial blood-stream infection (BSI) of any clinical specialty [1-4]. Interventions aimed at reducing HAI have succeeded in dramatically decreasing rates of infection in the US and have led the way for similar interventions in the UK, including the introduction of the Department of Health Saving Lives CVC care bundle in 2005 [5-8].

Monitoring of infection outcomes is vital for determining the impact of these interventions and for sustaining improvements in practice [9,10]. Comparison of healthcare associated BSI rates and assessment of variation of quality of care between PICUs would allow improved practices to be targeted at those most likely to benefit.

Reliable risk-adjustment is required for meaningful comparisons between PICUs [11]. At a national level, no single dataset accurately captures both clinical and microbiological BSI data [12]. Labbase2 is a national voluntary microbiological surveillance database collated by the Health Protection Agency (HPA), based on clinically significant isolates identified at laboratories serving NHS hospitals [13]. The Paediatric Intensive Care Audit Network (PICANet) collects data on all children admitted to PICUs in Britain, including clinical details such as diagnosis and morbidity score on admission [14]. Linkage of these existing datasets offers an efficient method for providing risk-adjusted national surveillance.

To demonstrate the effect of risk-adjustment using routinely collected data and the importance of standardised outcome measures, we linked PICANet data with microbiology data from two large UK PICUs, to assess reductions in BSI acquired within PICU.

METHODS

Data and case definition

Admission data for all children admitted to Birmingham Children's hospital (BCH) PICU (General and Cardiac) and Great Ormond Street Hospital (GOSH) PICU (General and Cardiac) between March 2003 and December 2010 were extracted from the PICANet database. Variables extracted for analysis were admission and discharge dates, Paediatric Index of Mortality (PIM2) score at admission, age, sex, admission type (planned or unplanned), admission source (same hospital or elsewhere), primary diagnosis at admission (based on primary diagnosis coded with the International Classification of Disease (ICD10)), and variables indicating renal support and mechanical ventilation [15].

BCH and GOSH laboratories routinely record microbiology data for all bacterial isolates from blood culture. From these laboratory systems, we extracted data on all positive isolates for children admitted to hospital between March 2003-2010, regardless of whether they were considered contaminants or clinically significant.

We defined an episode of BSI as any positive blood culture with:

1. One or more organisms isolated from any blood sample taken on the same day
2. Repeated samples with positive cultures of the same organism within 14 days

A child could have more than one BSI episode during an admission if different organisms were isolated on different days, or if the same organism was isolated on more than one day (>14 days apart).

We defined PICU-acquired BSI as any BSI from samples taken up to two days after discharge from PICU, but excluding samples taken on the day of admission or the day after admission to PICU. As laboratory records included the date but not the time the specimen was taken, some included samples may have been taken between 24 and 48 hours after admission to PICU, thereby possibly resulting in a slight overestimation of rates. Laboratory data after discharge from PICU was available for the majority of children (81%) as they were discharged to another ward within the same hospital.

We separately analysed PICU-acquired BSI due to skin and non-skin organisms, as we hypothesised that infection control practices might have more impact on BSI due to skin organisms, which can be acquired during invasive procedures or sample contamination [16,17]. Skin organisms were defined as coagulase negative staphylococcus, *Staphylococcus epidermidis*, *Corynebacterium* spp. or *Proprionibacterium* spp.. All other organisms were classified as non-skin organisms. PICU-acquired BSI episodes could include either skin organisms, non-skin organisms, or both, and so the number of episodes of PICU-acquired BSI due to skin organisms and due to non-skin organisms does not add up to the total number of episodes. We separately analysed PICU-acquired BSI in children staying >=48 hours to account for any differences in the number of very short-term admissions (with a lower risk of infection) between PICUs.

We assessed the effect of different case definitions for BSI reporting. The national voluntary surveillance system LabBase2, coordinated by the Health Protection Agency (HPA), requires reporting of clinically significant BSI. At one of the two laboratories, an additional variable indicated positive BSI that had been considered to be clinically significant and were reported to LabBase2, based on prospectively recorded consultant microbiologist opinion following regular meetings with the clinical team. At the other laboratory no classification of clinically significant BSI was available.

Data linkage

We generated our dataset by deterministic linkage of PICANet and microbiology records based on unique identifiers (NHS number, hospital number, name, date of birth and sex). Linkage was manually verified to ensure there were no false matches or missed matches.

Statistical analysis

PICU-acquired BSI rates were calculated as the number of PICU-acquired BSI per 1000 bed-days. Due to the low event rate, we assumed a log-linear trend and fitted Poisson regression models[1] to the data, with length of stay (in hours) as the exposure variable. Model fits were compared using Akaike's Information Criterion, goodness of fit tests and likelihood-ratio tests for nested models. Models with best-fit were used to identify significant risk-factors for PICU-acquired BSI from the patient characteristics extracted from PICANet (Table 1). For these models, the quarter-year of admission, age in months, and PIM2 score were treated as continuous variables. Quarter of year (3-month calendar period), sex, admission type, admission source, renal support, mechanical ventilation and diagnosis group (cardiovascular, respiratory, infection or other) were categorical variables. We aimed to evaluate how relatively simple risk-adjustment affects comparative measures rather than to inform direct comparisons between PICUs, as BSI risk-factors were limited within our data. A PICU-year interaction term was added to the model to test for differences in trends between PICUs. The two PICUs were randomly coded as PICU 1 and PICU 2 so that individual units were not identified (same coding used throughout analysis) and to deter erroneous conclusions about relative performance.

Incidence rate ratios (IRR) with 95% confidence intervals (CI) were derived from models of best fit and used to compare rates between PICUs. Risk-adjusted rates were derived for each PICU by adjusting for all risk-factors found to be significant in the Poisson regression. Kernel density estimates of rates were estimated for graphical display.

The time to infection was calculated as the number of days between admission and the date of PICU-acquired BSI. Cox proportional hazards models were fitted to the data to estimate the survival function for each PICU and to identify significant risk-factors for time to infection.

Analysis was performed using Stata 11 [18].

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[1] Full model: log(infections) = β_1 × quarter-year of admission + β_2 × PICU + β_3 × admission type + β_4 × diagnosis group + β_5 × renal support + β_6 × sex + β_7 × age + β_8 × PIM2 + β_9 × admission source + β_{10} × mechanical ventilation + β_{11} × quarter of year + log(length of stay)

RESULTS

13,376 records of bacterial isolates from blood culture dating between March 2003 and December 2010 inclusive were extracted from the microbiology systems at the two hospitals (n=5,589 PICU 1, n=7,787 PICU 2; hospital-wide). These corresponded to 6,842 episodes of BSI as defined in the case definition (hospital-wide).

Records for 20,924 admissions were extracted from the PICANet database for the two PICUs over the same time period, comprising a total of 117,800 bed days (approximately 15,000 bed-days or 2,600 admissions per year at the two PICUs combined). Table 1 shows the characteristics of the children admitted to the two PICUs between 2003-2010.

Table 1: PICANet data: characteristics of all children admitted to two PICUs in England, 2003-2010

Fig. 1 Probability of remaining free from PICU-acquired BSI in first 60 days of admission by PICU, adjusted for mechanical ventilation, age, PIM2, renal status, admission type, admission source, diagnosis group and quarter-year at admission.

PICU-acquired BSI

A total of 1,761 PICU-acquired BSI episodes were linked to 1,428 admissions. 144 (8.2%) of these BSI episodes included more than one type of organism isolated on the same day. 220 (15%) of these admissions had multiple PICU-acquired BSI episodes during their stay in PICU.

The rate of PICU-acquired BSI per 1000 bed-days was 15.17 (14.45-15.86) per 1000 bed-days (Table 2). Quarter-year of admission, quarter of calendar year, age, admission type, admission source, renal support, PICU and diagnosis group were found to be significant at the 5% level, but there was no evidence of an effect of sex, mechanical ventilation or PIM2 score on the rate of PICU-acquired BSI.

The crude IRR underestimated the difference between PICUs (1.15; 95% CI 1.05-1.26) and the IRR increased to 1.26 (95% CI 1.14-1.39) after adjusting for differences in significant risk-factors between PICUs. Although the median length of stay differed by PICU (70 and 48 hours in PICUs 1 and 2 respectively), the exclusion of short term admissions (<48 hours, n episodes=119) did not account for the difference between PICUs. The adjusted PICU IRR for admissions >=48 hours was 1.20 (95% CI 1.08-1.33). The median time to PICU-acquired infection was 7 days from admission (95% binomial CI 6-7). For any given time point, a greater proportion of children in PICU 2 had PICU-acquired BSI than in PICU 1, after adjusting for significant risk-factors (mechanical ventilation, age, PIM2, renal status, admission type, admission source, diagnosis group and quarter-year at admission (Figure 1)). Rates were lower in summer months.

The rate of PICU-acquired BSI decreased by 9% (95% CI 7%-11%) each year during the study period. This corresponded to a 44% reduction (a reduction of 7.54 per 1000 bed-days) in the rate of PICU-acquired BSI between 2003-2010. The percentage of admissions each year with PICU-acquired BSI decreased by 45% over the study period (from 8.3%-4.5% of admissions). There was no evidence of a difference in trends between PICUs (p-value=0.43 for trend-PICU interaction).

Table 2: Rate and risk-adjusted incidence rate ratios for PICU-acquired BSI. Incidence rate ratio for year of admission converted from IRR for quarter-year of admission

Skin organisms and Non-skin organisms

The rate of PICU-acquired BSI due to skin organisms was higher than the rate of PICU-acquired BSI due to non-skin organisms, and risk-factors for skin organisms differed to those for non-skin organisms (Table 3).

Rates of PICU-acquired BSI due to both skin organisms and due to non-skin organisms decreased between 2003-2010. As expected, there was a larger reduction seen in PICU-acquired BSI due to skin organisms (a 47% reduction of 5.00 per 1000 bed-days) compared with the decline due to non-skin organisms (a 34% reduction of 2.64 per 1000 bed-days). The percentage of admissions per year with PICU-acquired BSI due to skin organisms decreased by 52% (from 5.8-2.81) compared with 41% (from 3.6 to 2.1) due to non-skin organisms.

The difference between PICUs was due to differences in rates of non-skin organisms - there was no evidence of a difference in rates of skin organisms between PICUs (IRR = 1.10; 95% CI 0.97-1.25). The crude IRR for non-skin organisms underestimated the difference between PICUs (1.38; 95% CI 1.21-1.57), rising to 1.62 (95% CI 1.41-1.85) after adjusting for differences in population at risk between PICUs. Figure 3 shows the risk-adjusted rate of PICU-acquired BSI due to skin organisms and non-skin organisms in each PICU.

Fig. 2 Rates of PICU-acquired BSI due to skin organisms and non-skin organisms by PICU and quarter-year at admission, adjusted for quarter of year, admission type, admission source, age, renal support, diagnosis group . Symbols = Quarterly crude rates; Lines=Kernel density estimate of risk-adjusted trends

Table 3: Rates and risk-adjusted incidence rate ratios of PICU-acquired BSI due to skin organisms and non-skin organisms

Clinically significant BSI

Classification of BSI as clinically significant or not, based on prospectively recorded clinical opinion, was available for PICU 2. Of the 785 PICU-acquired BSI in this PICU, 321 (41%) were classified as clinically significant. This was largely due the number of coagulase negative staphylococcus classified as not clinically significant - of the 445 PICU-acquired BSI due to skin organisms, only 155 (34.5%) were clinically significant. However, a reduction in the number of non-skin organisms was also seen – of the 419 PICU-acquired BSI due to non-skin organisms, 284 (67.8%) were clinically significant.

The rate of clinically significant BSI was 7.39 (95% CI 6.58-8.18) per 1000 bed-days, compared with an overall rate of 18.05 (95% CI 16.80-19.32) for all PICU-acquired BSI at PICU 2 and 13.44 (95% CI 12.60-14.28) at PICU 1.

Figure 3 shows the rate of clinically significant and overall PICU-acquired BSI at PICU 2.

Fig. 3 Rates of clinically significant and all PICU-acquired BSI at PICU 2 by quarter-year at admission, adjusted for quarter of year, admission type, admission source, age, renal support and diagnosis group. Symbols = Quarterly crude rates; Lines=Kernel density estimate of risk-adjusted rates

DISCUSSION

Our study demonstrates the importance of risk-adjustment and standardised outcome measures for monitoring of changes in BSI rates within and between PICUs. We show that simple risk-adjustment can be achieved through linkage of routinely collected data. As variation between units is a key measure for monitoring the quality of care in PICU, these potential sources of bias need to be taken into account to ensure fair and accurate assessment of variation in outcomes [19].

This study spans a period when national and local guidance led to major changes in infection control and a near halving in rates of BSI. The dramatic reduction in PICU-acquired BSI rates seen from 2007, particularly in BSI due to skin organisms, corresponds to the introduction of the Saving Lives CVC care bundle [8]. These guidelines for insertion and maintenance of CVCs to prevent BSI led to the introduction of 2% chlorhexidine swabs at GOSH and infection control audits of hand hygiene and high impact interventions consistently scoring >90% in BCH. This is the first study to link microbiology data with hospital admissions and to quantify this reduction in PICUs, though such changes are well recognised by clinicians [20].

Although there is broad recognition of the importance of risk-adjustment, current PICU risk-adjustment scores for mortality (PIM2) or indicators of severity of illness (renal support, mechanical ventilation) do not accurately capture all risk-factors for BSI. There was no evidence of differing rates of PICU-acquired BSI due to skin organisms between units, suggesting that variation in rates of pathogens may be due to differences in PICU casemix that are not routinely captured. More detailed risk-factor information may further explain variation between PICUs and improvements in routine data quality and methodology will allow a wider range of risk-factors to be explored. Use of information on trajectories of care preceding PICU admission using longitudinal hospital administrative data may enhance risk-adjustment [21-24].

We identified large differences between rates of total BSI and clinically significant BSI for both skin and non-skin organisms. Although definitions for classification of healthcare-associated BSI exist, there are no clear criteria to guide clinical judgement on classification of clinically significant positive isolates that are reported to the national surveillance system LabBase2 [25-27]. Clinicians need to make daily judgements for the care and treatment of patients, but national monitoring requires objective outcome measures to achieve fair comparisons. Automated downloads of laboratory data to the voluntary surveillance system, introduced in recent years, offer the opportunity to capture all positive BSI data. Analysis based on these data would overestimate the total burden of clinically significant BSI acquired in PICU, as in our study. However, it is also important to monitor contamination, as this may lead to overtreatment and possible increased length of stay in PICU. Measuring all positive BSI would ensure valid comparisons, undistorted by variations in clinical opinion on clinical significance.

The success of risk-adjusted monitoring on a national scale will depend on a linkage infrastructure that ensures data quality and minimises error due to linkage of imperfect or incomplete identifiers, while allowing for standardised, risk-adjusted analyses of infection rates. Our analyses quantify substantial reductions in BSI rates in two PICUS, but a national system is required to identify units where further improvements are needed and to determine which practice innovations have most impact.

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Ethical approval

Collection of personally identifiable data has been approved by the National Information Governance Board (Formerly the Patient Information Advisory Group) http://www.nigb.nhs.uk/s251/registerapp and ethical approval granted by the Trent Medical Research Ethics Committee, ref. 05/MRE04/17. Consent for the use of the data in this study was obtained by the PICANet unit leads.

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TABLES

Table 1: PICANet data: characteristics of all children admitted to two PICUs in England, 2003-2010

		N admissions	%
Length of stay	<48 hours	9059	43.29
	>=48 hours	11865	56.71
Year of admission	2003	2361	11.28
	2004	2762	13.20
	2005	2423	11.58
	2006	2647	12.65
	2007	2638	12.61
	2008	2664	12.73
	2009	2936	14.03
	2010	2493	11.91
Quarter of year	Jan-Mar	4833	23.10
	Apr-Jun	5425	25.93
	Jul-Sep	5564	26.59
	Oct-Dec	5102	24.38
PICU	PICU 1	12310	58.83
	PICU 2	8614	41.17
Admission type	Planned	8583	41.02
	Unplanned	12341	58.98
Admission source	Same hospital	12772	61.04
	Elsewhere	8152	38.96
Diagnosis Group	Other	7163	34.23
	Cardiovascular	8493	40.59
	Respiratory	4600	21.98
	Infection	668	3.19
Renal support	No	20081	95.97
	Yes	843	4.03
Mechanical ventilation	No	16195	77.4
	Yes	4729	22.6
Sex	Female	11813	56.46
	Male	9110	43.54
	Unknown	1	0.00
Age group	<1 year	11347	54.23
	1-4 years	4839	23.13
	5-10 years	2611	12.48
	11-15 years	2127	10.17
Total		**20924**	

Table 2: Rate and risk-adjusted incidence rate ratios (IRRs) for PICU-acquired BSI. IRRs were adjusted for all significant risk-factors listed in the table and the IRR for year of admission was converted from the IRR for quarter-year of admission.

	PICU-acquired BSI		
Rate (95% CI) per 1000 bed-days	15.17 (14.45-15.86)		
% (95% CI) of admissions with BSI	6.82% (6.48%-7.17%)		
	N episodes	**Incidence rate ratio (95% CI)**	**p-value**
Year of admission		0.91 (0.89-0.93)	<0.001
Quarter of year			
Jan-Mar	472	1	
Apr-June	429	0.83 (0.73-0.95)	
Jul-Sep	410	0.83 (0.73-0.95)	
Oct-Dec	450	0.96 (0.85-1.10)	0.005
Age (months)		0.99 (0.99-0.99)	<0.001
PICU			
PICU 1	976	1	
PICU 2	785	1.26 (1.14-1.39)	<0.001
Admission type			
Planned	448	1	
Unplanned	1313	1.45 (1.28-1.64)	0.001
Admission source			
Same hospital	1007	1	
Elsewhere	754	0.72 (0.65-0.80)	<0.001
Diagnosis group			
Other	632	1	
Cardiovascular	601	0.81 (0.72-0.92)	
Respiratory	441	0.77 (0.68-0.87)	
Infection	87	1.26 (1.01-1.59)	<0.001
Renal support			
No	1482	1	
Yes	279	1.47 (1.29-1.68)	<0.001
Total	**1761**		

Table 3: Rates and risk-adjusted incidence rate ratios (IRRs) of PICU-acquired BSI due to skin organisms and non-skin organisms. IRRs were adjusted for all significant risk-factors listed in the table.

	Skin organisms			**Non-skin organisms**		
Rate (95% CI) per 1000 bed-days		9.29 (8.74-9.84)			7.37 (6.86-7.85)	
% (95% CI) of admissions with >=1 specimen		4.62% (4.34%-4.92%)			3.06% (2.83%-3.30%)	
	n	**Incidence rate ratio (95% CI)**	**p-value**	**n**	**Incidence rate ratio (95% CI)**	**p-value**
Year		0.90 (0.87-0.93)	<0.001		0.92 (0.89-0.94)	<0.001
Quarter						
Jan-Mar	290	1		227		
Apr-June	266	0.83 (0.71-0.99)		212	Not significant	0.230
Jul-Sep	250	0.82 (0.69-0.97)		200		
Oct-Dec	272	0.96 (0.81-1.14)	0.0457	216		
Age (months)		0.99 (0.99-0.99)	<0.001		0.99 (0.99-0.99)	<0.001
Admission source						
Same hospital	595	1		513	1	
Elsewhere	483	0.75 (0.66-0.86)	<0.001	342	0.70 (0.60-0.81)	<0.001
PICU						
PICU 1	633	1		436	1	
PICU 2	445	1.10 (0.97-1.25)	0.134	419	1.51 (1.31-1.74)	<0.001
Admission type						
Planned	272	1		229	1	
Unplanned	806	1.39 (1.20-1.63)	<0.001	626	1.25 (1.04-1.51)	0.015
Diagnosis group						
Other	406	1		289	1	
Cardiovascular	338	0.70 (0.60-0.81)		310	0.87 (0.73-1.04)	
Respiratory	301	0.81 (0.70-0.94)		195	0.75 (0.62-0.90)	
Infection	33	0.75 (0.52-1.07)	<0.001	61	2.00 (1.52-2.66)	<0.001
Renal support						
No	921	1		709	1	
Yes	157	1.42 (1.19-1.68)	<0.001	146	1.53 (1.28-1.84)	0.001
Mechanical Ventilation						
Yes	192	Not significant		180	1	
No	886			675	0.75 (0.63-0.90)	0.002
PIM2		Not significant			1.67 (1.08-2.57)	0.021
Total	**1078**			**855**		

FIGURES

Fig. 1 Probability of remaining free from PICU-acquired BSI in first 60 days of admission by PICU, adjusted for mechanical ventilation, age, PIM2, renal status, admission type, admission source, diagnosis group and quarter-year at admission.

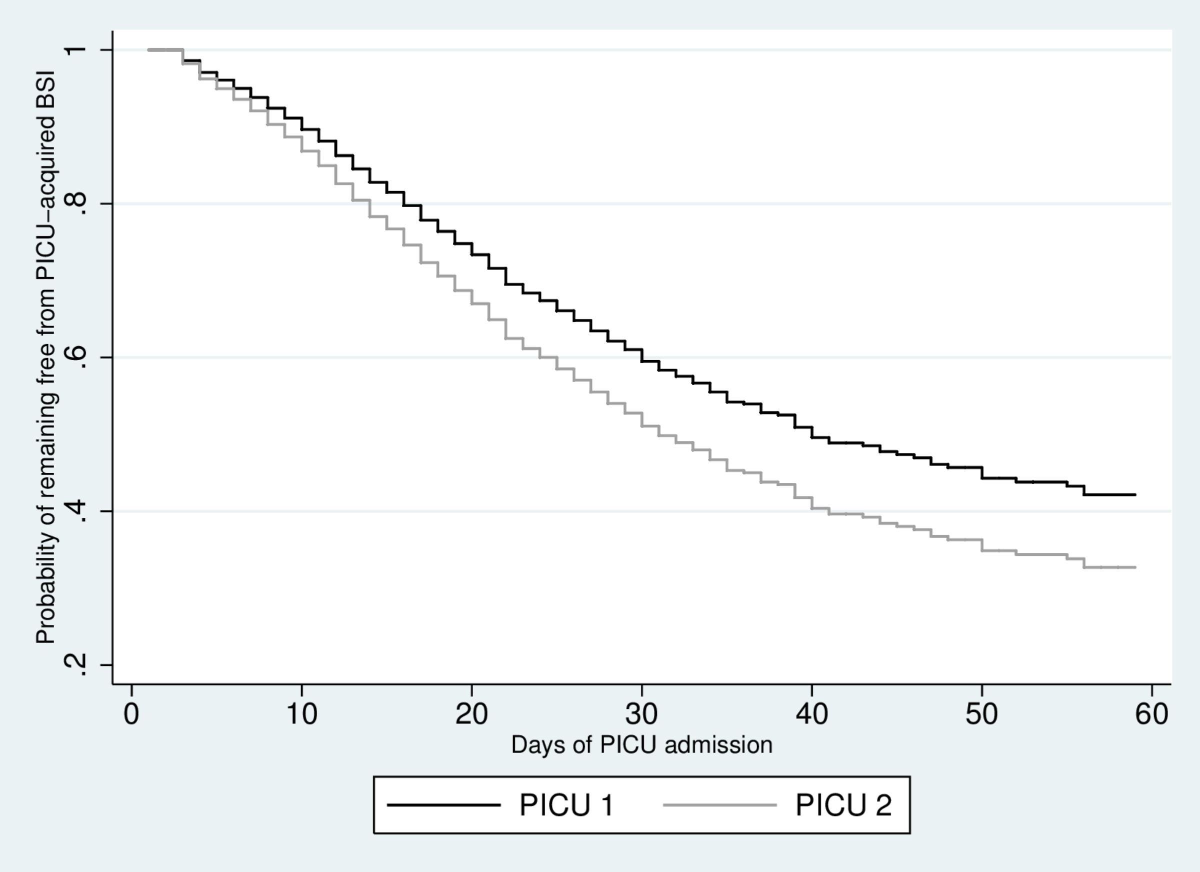

Fig. 2 Rates of PICU-acquired BSI due to skin organisms and non-skin organisms by PICU and quarter-year at admission, adjusted for quarter of year, admission type, admission source, age, renal support and diagnosis group. Symbols = Quarterly crude rates; Lines=Kernel density estimate of risk-adjusted trends

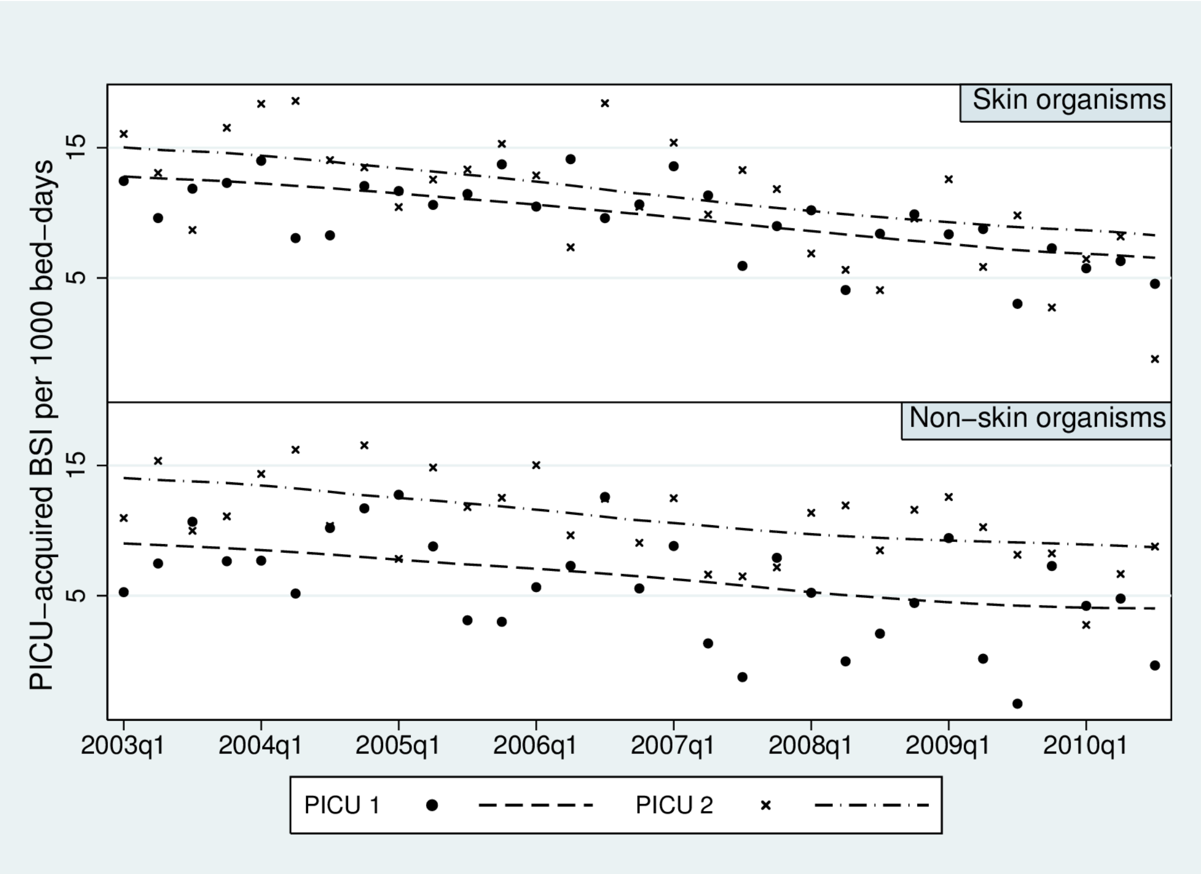

Fig. 3 Rates of clinically significant and all PICU-acquired BSI at PICU 2 by quarter-year at admission, adjusted for quarter of year, admission type, admission source, age, renal support and diagnosis group. Symbols = Quarterly crude rates; Lines=Kernel density estimate of risk-adjusted rates