
Article:
Fraser, Lorna Katharine orcid.org/0000-0002-1360-4191 and Parslow, Roger (2017) Children with Life-Limiting Conditions in Paediatric Intensive Care Units: : a national cohort, data linkage study. Archives of Disease in Childhood. pp. 1-9. ISSN 1468-2044

https://doi.org/10.1136/ archdischild- 2017- 312638

Children with Life-Limiting Conditions in Paediatric Intensive Care Units: a national cohort, data linkage study

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Key words

PICU

Life-Limiting Condition

Palliative Care

Survival

Child

Tables 3; Figures 2

Word count abstract 246; main body 2603

Short Running Title: Children with life-limiting conditions in PICU

What is known: The prevalence of children and young people with a life-limiting (LLC) or life-threatening conditions (LTC) is rising. Overall mortality in PICU is decreasing.

What this study adds:

Children with a LLC accounted for the majority of admissions, bed-days and deaths in PICU. They were 75% more likely to die in PICU and there was 93% survival at one year for children with a LLC.

Abstract

Objective

To determine how many children are admitted to paediatric intensive care (PICU) with life-limiting conditions (LLC) and their outcomes.

Design

National cohort , data-linkage study

Setting

PICUs in England

Patients

Children admitted to a UK PICU (1st Jan 2004 and 31st March 2015) were identified in the Paediatric Intensive Care Audit Network dataset. Linkage to hospital episodes statistics enabled identification of children with a LLC using an International Classification of Diseases (ICD10) codelist.

Main Outcome Measures

Random effects logistic regression was undertaken to assess risk of death in PICU. Flexible parametric survival modelling was used to assess survival in the year after discharge.

Results

Overall 57.6% (n=89,127) of PICU admissions and 72.90% (n=4821) of deaths in PICU were for an individual with a LLC.

The crude mortality rate in PICU was 5.4% for those with a LLC and 2.7% of those without a LLC. In the fully adjusted model, children with a LLC were 75% more likely than those without a LLC to die in PICU (OR 1.75 (95%CI 1.64-1.87)).

Although overall survival to one year post discharge was 96%, children with a LLC were 2.5 times morelikely to die in that year than children without a LLC (OR 2.59 (95%CI 2.47-2.71)).

Conclusions

Children with a LLC accounted for a large proportion of the PICU population. There is an opportunity to integrate specialist paediatric palliative care services with paediatric critical care to enable choice around place of care for these children and families.

Introduction

Life-limiting conditions (LLC) are those for which there is no reasonable hope of cure and from which children will ultimately die, e.g. Duchenne Muscular Dystrophy or neurodegenerative disease. Life-threatening conditions (LTC) are those for which curative treatment may be feasible but can fail, e.g. cancer. LLC will be used to include life-limiting and life-threatening conditions.

The prevalence of children and young people (CYP) with a LLC is increasing [1] partly due to more aggressive treatment of complications and the use of medical technologies, including Paediatric Intensive Care (PICU). These children often have repeated hospital admissions [2] and use increasing amounts of hospital resources [3-5]. Many of these children also die on PICU [6] when treatment fails or is withdrawn. This study aims to ascertain what proportion of admissions to PICUs are for children with a LLC and their outcomes in PICU and up to one year post discharge.

Methods

Datasets

The Paediatric Intensive Care Audit Network (PICANet) collects data on all children admitted to PICUs in the UK and Ireland. All admissions to a PICU in the UK between 1/1/2004 and 31/3/2015 were identified in the PICANet dataset [7]. Only children resident in England were included as only their inpatient hospital data (Hospital Episodes Statistics (HES)) were available for linkage [8]. Hospital data for the other nations of the UK were not available.

The Office for National Statistics (ONS) death record data in England were available with a censor date of 1/11/2015 [9].

Linkage of the PICANet dataset to the HES and ONS data was undertaken by the NHS Digital [10]. The standard deterministic linkage algorithm using NHS number, date of birth, sex and postcode were used.

Clinical variables

Inpatient HES data

The PICANet data is of high quality and validated but some of the non-mandatory fields, including co-morbidities, are incomplete. Therefore it is not possible to identify children with a LLC using the PICANet dataset alone. Linkage to the inpatient HES data (1/4/1997-31/3/2015) enabled the use of a previously developed International Classification of Diseases (ICD10) coding framework [1] to identify individuals with a LLC (Supplementary Table 1). A PICU admission was categorised with a LLC if one of the LLC codes were recorded within the HES data for that individual before the date of PICU discharge. For the analyses for survival in the year after PICU discharge LLC codes up to the censor date were included.

PICANet data

Clinical diagnoses were coded using Clinical Terms 3 and aggregated into 12 primary diagnostic groups [11].

Risk adjustment for mortality used the log odds of mortality based on the Paediatric Index of Mortality (PIM2) with recalibrated coefficients calculated using data from 2011-13 [12]. PIM2 was categorised into five categories of risk <1%, 1-<5%, 5-<15%, 15-<30%, 30%+.

Length of stay was categorised into <1 day, 1-< 3 days, 3-<7 days, 7-<14 days, 14-<28 days and ≥ 28 days. The total number of bed-days for each individual was calculated for all their PICU admissions. The number of PICU admissions were categorised as single admission, two admissions, three admissions, four or more admissions.

The type of admission was defined as planned after surgery, unplanned after surgery, planned other and unplanned.

ONS Death Data

Date of death was obtained from the ONS data [9].

Socio-demographic variables

Age at admission to PICU was categorized as <1 year, 1–4 years, 5–10 years, 11–15 years, ≥16 years. Sex was included in the analysis only where it was non-ambiguous.

An Index of Multiple Deprivation (IMD)[13] category was assigned to each individual based upon their Lower Super Output Area (LSOA) of residence. An LSOA is a census geographical area built up of Output Areas with population of 1000–3000 per LSOA [14].

Ethnicity is poorly recorded in all the datasets therefore ethnicity was determined using two name analysis programs which classified children as South Asian (Pakistani, Indian, Bangladeshi): Nam Pehchan [15, 16] and the South Asian Names and Group Recognition Algorithm [17]. The results were corrected manually for known misclassification errors [18]. Ethnicity was assessed as South Asian or not as the South Asian population are the largest minority ethnic group in the UK(REF).

Statistical Analyses

Descriptive statistics were undertaken and differences between groups assessed by chi-squared or t-test.

Random effects logistic regression was undertaken to account for inter PICU variation in the outcome; death in PICU. Variables were included via a forced entry method and retained if $p<0.05$ or if they improved the model fit assessed using the Bayesian information criterion (BIC).

Flexible parametric survival modelling was undertaken to assess survival in the year after discharge from PICU rather than traditional cox regression as the proportional hazards assumption was violated [19]. Data from the last PICU admission for each individual discharged alive from PICU were included.

Analyses were carried out using STATA version 13, and tests of statistical significance were at $p\leq0.05$.

Ethics approval

Collection of personally identifiable data has been approved by the Patient Information Advisory Group (now the Health Research Authority Confidentiality Advisory Group) see -

http://www.hra.nhs.uk/documents/2015/12/piag-register-8.xls - and ethics approval granted by the Trent Medical Research Ethics Committee, ref. 05/MRE04/17 +5.

Results

Cohort and Linkage

Nearly 200,000 PICU admissions occurred in the UK in the study period. After excluding non-English residents and those with poor quality demographic data[1], data for 103,374 individuals were sent for linkage. Linkage was successful for 102,722 individuals (99%) who had 154,667 PICU admissions (Figure 1).

There were no significant differences between those who linked and those in whom linkage was not successful by sex, ethnicity, PIM2 score or length of PICU stay (Supplementary Table 2). Some significant differences were found; linkage improved from 98.0% in 2004 to 99.4% in 2015 (chi2 365, p<0.001), fewer >16 year olds linked compared to the < 1 year olds (98.9% vs 99.3%) and children with more PICU admissions were more likely to be linked than those with a single admission (99.5% vs 98.9% chi2 120, p<0.001).

Descriptive Statistics

Overall 57.6% (n=89127) of PICU admissions were for an individual with a LLC (Table 1). Excluding 2015 data which in only part year, the percentage of admissions to PICU for those with a LLC has increased from 51.8% to 61.0%. There was a U shaped association with age with 58.5% of the under 1 year olds admitted to PICU having a LLC, 50.2% of the 11-15 year olds and 65.4% of the >16 year olds. More of the admissions from children with a South Asian background had a LLC compared to non-South Asians (62.9% vs 56.9% chi2=233, p<0.001).

[1] Poor quality demographic data = missing NHS number and date of birth which are required for linkage

Differences between the two groups existed for the clinical variables with 94.1% of those children whose reason for PICU admission was multisystem having a LLC compared with only 8.8% of trauma cases and 43.3% of infective cases (chi2 1300, p<0.001).

The risk of mortality scores varied by LLC status with. 52.3% of those with a PIM 2 score <1% had a LLC, 77.8% of those with a PIM 2 score of 15-<30% and 62.3% of those with a PIM 2 score of >30% (chi2 2300, p<0.001).

A linear association with length of PICU stay was shown with 49.6% of those with a PICU stay of <1 day and 87.5% of those staying in PICU >28 days having a LLC (chi2 6000, p<0.001). The median length of stay was 2.6 days (IQR 1.0,6.1) for those with a LLC compared to 1.6 days (IQR 0.8,3.5) for those without a LLC.

The total number of PICU bed days for this cohort was 763,664; children with a LLC accounted for 72.6% (554,404).

More than 66% of the planned PICU admissions after surgery were for children with a LLC compared to 51.6% of unplanned PICU admissions (chi2 3600, p<0.001).

Deaths

11,588 children had died at the censor date, with 6612 deaths occurring in PICU. Children with a LLC accounted for 72.9% (n=4821) of PICU deaths and 87.4% (n= 4397) of deaths after discharge. The crude PICU mortality rate was 5.4% for those with a LLC and 2.7% for those without a LLC.

Death in PICU

The unadjusted risk of death in PICU for children with a LLC was nearly twice that of those without a LLC (OR 1.94 (95%CI 1.84,2.06)). After adjusting for expected risk of mortality and other clinical and demographic variables, children with a LLC were 75% more likely than those without a LLC to die in PICU (OR 1.75 (95%CI 1.64-1.87))(Table 2).

Stratified analyses by LLC status highlighted some differences between the main variables associated with a higher risk of death in PICU (Supplementary Table 3a and 3b). For those with a LLC , being older than age 16 years (OR 1.37 (95%CI 1.12-1.67)) and of South Asian origin (OR 1.30 (95%CI 1.20-1.41)) had a higher risk of death. This was not seen for those without a LLC. The diagnoses with highest risk of death in PICU were blood and lymph (OR 2.54 (95%CI 1.98-3.25)) or endocrince/metabolic (OR 2.38 (95%CI 2.05-2.76)) for those with a LLC compared to trauma (OR 2.37 (95%CI 1.84-3.00)) or neurological conditions (OR 2.19 (95%CI 1.79-2.69)) for those without a LLC. The risk of death was highest for stays longer than 7 days in those with a LLC but not until 14 days for those without a LLC.

The odds of dying in PICU decreased by 3% each year (OR 0.98 (95%CI 0.97-0.99)).

Survival after discharge from PICU

Overall survival rate is >96% at one year after PICU (figure 2a). There are differences between these survival functions for children with (Figure 2b) and without a LLC (Figure 2c). There is a steeper curve in the first 3 months after discharge from PICU for those with a LLC with approx. 93% still alive at one year post discharge. For those without a LLC the survival curve is much flatter and > 99% are alive at one year post PICU discharge.

A lognormal distribution model with 5 degrees of freedom provided the best fit assessed using BIC (Table 3).There are some similarities to the death in PICU model: children with a LLC ((OR 2.59 (95%CI 2.47-2.71)), those from a South Asian background (OR 1.19 (95%CI 1.13-1.25)) and those from the most deprived category (OR 1.08 (95%CI 1.02-1.14) were more likely to die in the year after discharge from PICU than children without a LLC, non South-Asian and those in the least deprived areas respectively. All other types of PICU admission had significantly higher odds of death compared to the planned after surgery group and the odds of dying after discharge decreased by 3% with each increasing year of admission (OR 0.97 (95%CI 0.96-0.98)). Compared to the reference

group of respiratory reasons for PICU admission, those with an oncology (OR 1.83 (95%CI 1.70-1.97)) or neurology diagnoses (OR 1.17 (95%CI 1.11-1.24)) were more likely to die in the year after discharge from PICU. Those with trauma (OR 0.63 (95%CI 0.53-0.77)), or body wall and cavities (OR 0.63 (95%CI 0.54-0.72)) diagnoses were significantly less likely to die in the year after discharge from PICU.

In contrast to the in-PICU death models, all those aged 1- 15 years were significantly less likely to die than the <1 age group.

Discussion

Children with a LLC accounted for nearly 58% of all admissions to PICU, 72% of PICU bed-days and 87.5% of all PICU admissions that lasted > 28 days. Although the mortality rate continues to decrease in PICU, 73% of all deaths in PICU during this study were in children with a LLC. The survival in the year after PICU discharge was also significantly lower in children with a LLC compared to those without a LLC.

The high number and percentage of PICU admissions for children with a LLC is similar to results from a US study in which children with complex chronic conditions (CCC) accounted for 53% (range 22.4-70.6%) of PICU admissions [20]. The definitions used to identify the populations with CCC were different to the LLC definition used in the current study. A multi country prevalence study found that 67% of children had a CCC or disability within PICU or NICU [21].

Previous work has found that children with a CCC had an increased risk of prolonged length of PICU stay (>15 days) [20] and children who died in PICU have longer lengths of stay before death [22]. This study has shown that the risk of death in PICU is significantly higher for those with a LLC who have been in PICU for longer than 7 days.

The higher PICU crude death rate for children with a LLC is not unexpected and confirms the patterns seen in the US study where they found in-PICU mortality of 3.9% for those with a CCC

compared to 2.2% for children with no chronic condition and 0.3% for those with non-complex chronic conditions [20]. However, death in a child with a LLC may be expected and admissions to PICU are known to be stressful [23-26] and parents and siblings of children who died in hospital show more psychological symptoms [27] and poorer adjustment [28] than if their child had died at home. If the child is likely to die despite PICU admission then an alternative place of care such as being cared for at home or in a hospice by specialist paediatric palliative care may be more appropriate. Guidance from The European Association of Palliative Care [29] and the International Children's Palliative Care Network [30] both state that the family home should, where possible, be the main place of care and that these families should have access to paediatric palliative care services.

With in-PICU mortality falling to low levels it is important that other in/post PICU outcomes such as quality of life or functional status are assessed, especially for this group of children with high care needs.

Although the vast majority of children survived their PICU admission, nearly 7% of those with a LLC will die in the year after discharge from PICU with many of these deaths occurring in the first 3 months. PICU staff are highly experienced at caring for a dying child and their family but given the expansion of specialist paediatric palliative care services and the children's hospice sector over the last decade further integration of these services may offer the family more choice over place of care or death for their child and can often offer longer term input, both when the child has died and in the bereavement period than is possible from a PICU.

Strengths/Limitations

This is the first national study providing data on survival following PICU admission in this population of children and it utilised linked audit, administrative and hospital data. Identification of children with a LLC in this dataset was via the HES data. This is an administrative dataset in which the coding

has improved over time but its primary aim is not as a research dataset. Lack of agreement on definitions of some complex conditions has been shown previously [31]. Having complete data for co-morbidities in the PICANet dataset, which is audited for quality, would be preferable.

Conclusions

Children with a LLC accounted for nearly 58% of admissions to PICU, 72% of bed-days, 87.5% of stays greater than 28 days and 73% of deaths in PICU. There is an opportunity, given the recent growth in specialist paediatric palliative care services, to have integration of these services to enable choice around place of care and place of death for these children and families.

Future studies collecting high quality information on changes in functional status and quality of life is vital to further gauge the clinical value of these PICU admissions.

Acknowledgements

The PICANet Audit is commissioned by the Healthcare Quality Improvement Partnership (HQIP) as part of the National Clinical Audit Programme (NCA). HQIP is led by a consortium of the Academy of Medical Royal Colleges, the Royal College of Nursing and National Voices. Its aim is to promote quality improvement, and in particular to increase the impact that clinical audit has on healthcare quality in England and Wales. HQIP holds the contract to manage and develop the NCA Programme, comprising more than 30 clinical audits that cover care provided to people with a wide range of medical, surgical and mental health conditions. The PICANet Audit is funded by NHS England, the Welsh Government, NHS Lothian/National Service Division NHS Scotland, the Royal Belfast Hospital for Sick Children, The National Office of Clinical Audit (NOCA), Republic of Ireland and HCA Healthcare.

Conflicts of Interest Statement

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Funding

This paper is independent research arising from a Postdoctoral Fellowship supported by the National Institute for Health Research. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

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Archives of Disease in Childhood 2011;**96:**922-926.

Table 1 Descriptive Statistics of PICU Admissions by LLC Status (with row %)

	Total	LLC		No LLC		x^2	P value
Number	154,667	89127	*57.6*	65540	*42.4*		
Age Category						556	<0.001
<1 year	72,170	42,232	*58.5*	29,938	*41.5*		
1-4 years	39,571	23,097	*58.4*	16,474	*41.6*		
5-10 years	20,448	11,982	*58.6*	8,466	*41.4*		
11-15 years	19,003	9,542	*50.2*	9,461	*49.8*		
16+	3,467	2,267	*65.4*	1,200	*34.6*		
missing	8	7		1			
Sex						3.1	0.21
Male	87,686	50,422	*57.5*	37,264	*42.5*		
Female	66,933	38,682	*57.8*	28,251	*42.2*		
missing	48	23		25			
Ethnicity						233	<0.001
Non South Asian	136,670	77,804	*56.9*	58,866	*43.1*		
South Asian	17,997	11,323	*62.9*	6,674	*37.1*		
Deprivation Category						74.7	<0.001
Category 1 (least deprived)	21,421	12,101	*56.5*	9,320	*43.5*		
Category 2	21,816	12,573	*57.6*	9,243	*42.4*		
Category 3	26,341	15,437	*58.6*	10,904	*41.4*		
Category 4	34,498	19,935	*57.8*	14,563	*42.2*		
Category 5 (most deprived)	49,538	28,361	*57.3*	21,177	*42.7*		
missing	1,053	720		333			
Diagnostic Group (reason for PICU admission)						1300	<0.001
Neurological	17,270	8,154	*47.2*	9,116	*52.8*		
Cardiac	44,767	32,465	*72.5*	12,302	*27.5*		
Respiratory	42,230	21,687	*51.4*	20,543	*48.6*		
Oncology	5,190	4,663	*89.8*	527	*10.2*		
Infection	8,014	3,468	*43.3*	4,546	*56.7*		
Musculoskeletal	5,736	3,192	*55.6*	2,544	*44.4*		
Gastrointestinal	10,019	5,245	*52.4*	4,774	*47.6*		
Other	8,140	4,554	*55.9*	3,586	*44.1*		
Blood and lymph	1,456	757	*52.0*	699	*48.0*		
Trauma	4,581	405	*8.8*	4,176	*91.2*		
Endocrine/metabolic	3,878	2,131	*55.0*	1,747	*45.0*		
Multisystem	427	402	*94.1*	25	*5.9*		
Body wall and cavities	2,959	2,004	*67.7*	808	*32.3*		
Risk of Mortality (PIM 2)						2001	<0.001
<1%	48,957	25,583	*52.3*	23,374	*47.7*		
1-<5%	74,212	42,403	*57.1*	31,809	*42.9*		
5-<15%	24,727	16,261	*65.8*	8,466	*34.2*		
15-<30%	4,270	3,321	*77.8*	949	*22.2*		
>30%	2,501	1,559	*62.3*	942	*37.7*		
LOS PICU (days)						5600	<0.001
<1	45,246	22,420	*49.6*	22,826	*50.4*		
1 to <3	49,285	26,579	*53.9*	22,706	*46.1*		
3 to <7	34,122	20,381	*59.7*	13,741	*40.3*		

7 to <14	15,957	11,342	*71.1*	4,615	*28.9*		
14 to <28	6,603	5,401	*81.8*	1,202	*18.2*		
28+	3,412	2,986	*87.5*	426	*12.5*		
missing	42	18	*42.9*	24	*57.1*		
Type of PICU admission						3600	<0.001
Planned - after surgery	49,749	33,034	*66.4*	16,715	*33.6*		
Unplanned after surgery	7,688	3,985	*51.8*	3,703	*48.2*		
Planned other	10,900	7,551	*69.3*	3,349	*30.7*		
Unplanned	86,050	44,412	*51.6*	41,638	*48.4*		
Not known	280	145		135			
Year of PICU admission						574	<0.001
2004	12,293	6,366	*51.8*	5,927	*48.2*		
2005	12,326	6,531	*53.0*	5,795	*47.0*		
2006	12,634	7,116	*56.3*	5,518	*43.7*		
2007	13,275	7,492	*56.4*	5,783	*43.6*		
2008	13,462	7,463	*55.4*	5,999	*44.6*		
2009	14,023	7,994	*57.0*	6,029	*43.0*		
2010	14,185	8,341	*58.8*	5,844	*41.2*		
2011	14,006	8,282	*59.1*	5,724	*40.9*		
2012	14,597	8,904	*61.0*	5,693	*39.0*		
2013	14,865	9,126	*61.4*	5,739	*38.6*		
2014	14,973	9,137	*61.0*	5,836	*39.0*		
2015	4,028	2,375	*59.0*	1,653	*41.0*		

Table 2 Random Effects Logistic Regression Model for Death in PICU

[n=153,513, group = 35, wald chi2=10213, BIC= 40229, sigma_u=0.30, rho=0.03]

	Odds Ratio	**95% Confidence Intervals**		**p-value**
LLC				
No	REF			
Yes	1.75	1.64	1.87	<0.001
Age Category				
<1 year	REF			
1-4 years	0.81	0.75	0.87	<0.001
5-10 years	0.94	0.86	1.03	0.20
11-15 years	1.06	0.96	1.16	0.26
16+	1.37	1.13	1.66	<0.001
Sex				
Male	REF			
Female	1.09	1.03	1.15	0.002
Ethnicity				
Non South Asian	REF			
South Asian	1.30	1.20	1.41	<0.001
Deprivation Category				
Category 1 (least deprived)	REF			
Category 2	1.02	0.91	1.13	0.77
Category 3	1.03	0.92	1.14	0.64
Category 4	1.07	0.97	1.18	0.18
Category 5 (most deprived)	1.07	0.97	1.17	0.17
Diagnostic Group (reason for PICU admission)				
Neurological	1.39	1.26	1.54	<0.001
Cardiac	1.23	1.13	1.35	0.001
Respiratory	REF			
Oncology	2.06	1.75	2.42	<0.001
Infection	1.94	1.74	2.17	<0.001
Musculoskeletal	0.74	0.55	0.99	0.04
Gastrointestinal	1.39	1.22	1.58	<0.001
Other	1.26	1.10	1.45	<0.001
Blood and lymph	2.32	1.86	2.91	<0.001
Trauma	1.69	1.43	2.01	<0.001
Endocrine/metabolic	2.18	1.90	2.50	<0.001
Multisystem	0.67	0.33	1.38	0.28
Body wall and cavities	0.97	0.76	1.22	0.78
Risk of Mortality (PIM 2)				
<1%	REF			
1-<5%	4.54	3.91	5.28	<0.001
5-<15%	12.46	10.65	14.57	<0.001
15-<30%	32.56	27.44	38.64	<0.001
>30%	201.63	169.60	239.70	<0.001
LOS PICU (days)				
<1	1.51	1.39	1.63	<0.001
1 to <3	REF			

3 to <7	0.86	0.79	0.94	0.001
7 to <14	1.09	0.99	1.20	0.07
14 to <28	2.02	1.81	2.24	<0.001
>28	3.98	3.53	4.47	<0.001
Type of PICU admission				
Planned - after surgery	REF			
Unplanned after surgery	1.20	1.01	1.42	0.04
Planned other	1.32	1.14	1.52	<0.001
Unplanned	1.53	1.38	1.70	<0.001
Not known	1.35	0.63	2.88	0.44
Year of Admission	0.97	0.96	0.98	<0.001

Table 3 Results of Flexible parametric survival modelling for survival to 365 days after discharge from PICU

[n=91,614]

	Hazard Ratio	95% Confidence Intervals		p-value
Age Category				
<1 year	REF			
1-4 years	0.83	0.80	0.87	<0.001
5-10 years	0.77	0.73	0.82	<0.001
11-15 years	0.85	0.80	0.90	<0.001
16+	0.98	0.89	1.09	0.72
Sex				
Male	REF			
Female	1.02	0.99	1.06	0.23
Ethnicity				
Non South Asian	REF			
South Asian	1.19	1.13	1.25	<0.001
Deprivation Category				
Category 1 (least deprived)	REF			
Category 2	0.99	0.92	1.05	0.66
Category 3	1.03	0.96	1.09	0.41
Category 4	1.06	1.00	1.13	0.04
Category 5 (most deprived)	1.08	1.02	1.14	0.01
LLC				
No	REF			
Yes	2.59	2.47	2.71	<0.001
Diagnostic Group (reason for PICU admission)				
Neurological	1.17	1.11	1.24	<0.001
Cardiac	0.86	0.81	0.90	<0.001
Respiratory	REF			
Oncology	1.83	1.70	1.97	<0.001
Infection	0.87	0.80	0.94	0.001
Musculoskeletal	0.91	0.81	1.03	0.152
Gastrointestinal	1.04	0.97	1.12	0.276
Other	1.04	0.96	1.13	0.339
Blood and lymph	0.98	0.82	1.17	0.79
Trauma	0.63	0.53	0.77	<0.001
Endocrine/metabolic	1.08	0.98	1.20	0.117
Multisystem	0.97	0.70	1.33	0.831
Body wall and cavities	0.63	0.54	0.72	<0.001
Risk of Mortality (PIM 2)				
<1%	REF			
1-<5%	1.28	1.22	1.35	<0.001
5-<15%	1.55	1.45	1.64	<0.001
15-<30%	2.07	1.88	2.28	<0.001
>30%	2.46	2.12	2.85	<0.001
LOS PICU (days)				
<1	1.14	1.08	1.19	<0.001

1 to <3	REF			
3 to <7	1.06	1.01	1.12	0.01
7 to <14	1.29	1.22	1.37	<0.001
14 to <28	1.58	1.47	1.71	<0.001
>28	1.75	1.57	1.95	<0.001
Type of PICU admission				
Planned - after surgery	REF			
Unplanned after surgery	1.22	1.12	1.33	<0.001
Planned other	1.65	1.54	1.78	<0.001
Unplanned	1.37	1.29	1.44	<0.001
Not known	1.17	0.76	1.78	0.48
Year of Admission	0.97	0.96	0.98	<0.001

Figure 1 Study Flowchart

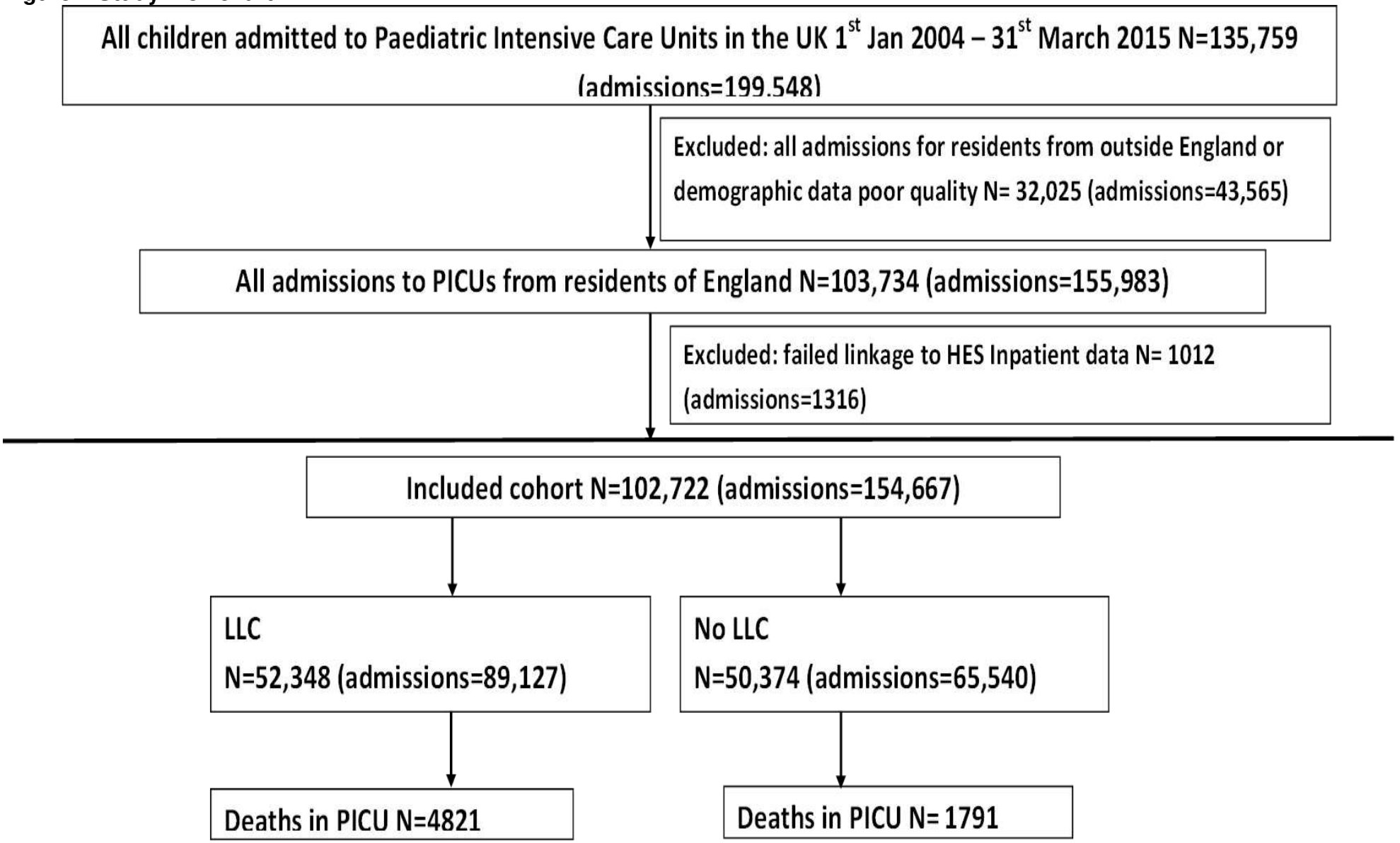


Figure 2 Survival Curves with 95% Confidence intervals

Figure 2a

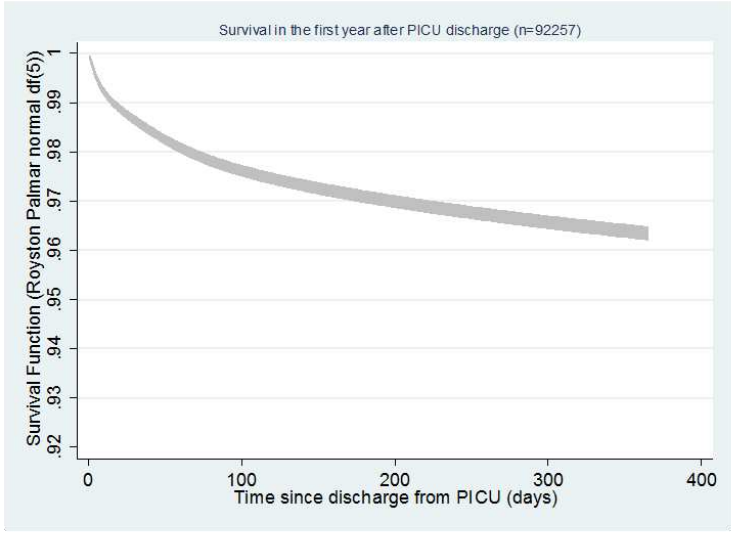


Figure 2b

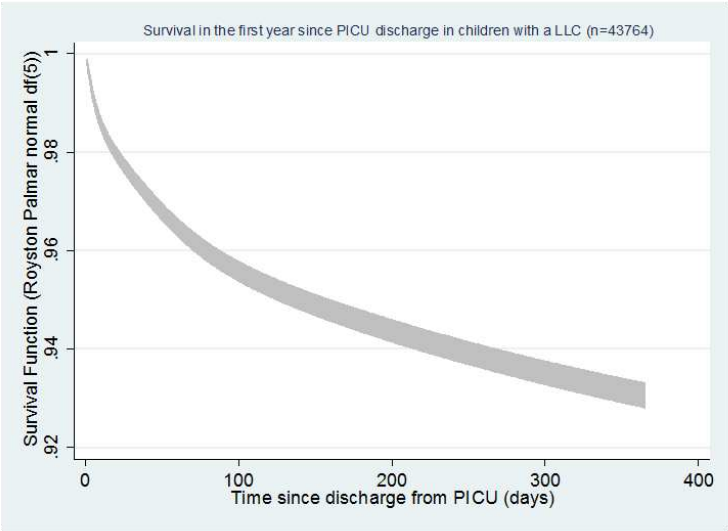
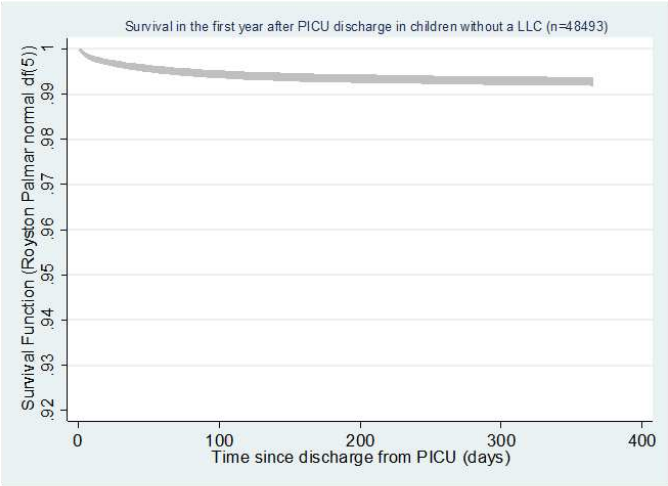


Figure 2c



Supplemental Table 1 ICD10 FILTER CODES to IDENTIFY LIFELIMTING DIAGNOSES IN CHILDREN & YOUNG PEOPLE

A	**B**	**C**	**D**	**E**	**F**	**G**	**G**	**H**	**I**	**J**
A17	B20-B24	C00-C97	D33	E31.0	F80.3	G10	G82.3	H11.1	I21	J84.1
A81.0			D43	E34.8	F84.2	G11.1	G82.4	H49.8	I27.0	J96
A81.1			D44.4	E70.2		G11.3	G82.5	H35.5	I42	J98.4
			D48	E71		G12	G93.4		I61.3	
			D56.1	E72		G20	G93.6		I81	
			D61.0	E74		G23.0	G93.7			
			D61.9	E75		G23.8				
			D70	E76		G31.8				
			D76.1	E77		G31.9				
			D81	E79.1		G35				
			D82.1	E83.0		G40.4				
			D83	E84		G40.5				
			D89.1	E88.0		G60.0				
				E88.1		G60.1				
						G70.2				
						G70.9				
						G71.0				
						G71.1				
						G71.2				
						G71.3				
						G80.0				
						G80.8				
K	**L**	**N**	**P**	**Q**	**Q**	**Q**	**Q**	**Q**	**T**	**Z**
K55.0	M31.3	N17	P10.1	Q00.0	Q21.8	Q39.6	Q78.0	Q93.2	T86.0	Z51.5
K55.9	M32.1	N18	P11.2	Q01	Q22.0	Q41.0	Q78.5	Q93.3	T86.2	
K72	M89.5	N19	P21.0	Q03.1	Q22.1	Q41.9	Q79.2	Q93.4		
K74		N25.8	P28.5	Q03.9	Q22.4	Q43.7	Q79.3	Q93.5		
K76.5			P29.0	Q04.0	Q22.5	Q44.2	Q80.4	Q93.8		
K86.8			P29.3	Q04.2	Q22.6	Q74.8	Q81	Q95.2		
			P35.0	Q04.3	Q23.0	Q44.5	Q82.1			
			P35.1	Q04.4	Q23.4	Q44.7	Q82.4			
			P35.8	Q04.6	Q23.9	Q60.1	Q85.8			
			P37.1	Q04.9	Q25.4	Q60.6	Q86.0			

			P52.4 P52.5 P52.9 P83.2 P91.2 P91.6 P96.0	Q07.0 Q20.0 Q20.3 Q20.4 Q20.6 Q20.8 Q21.3 Q23.2	Q25.6 Q26.2 Q26.4 Q26.8 Q28.2 Q32.1 Q33.6	Q61.4 Q61.9 Q64.2 Q74.3 Q75.0 Q77.2 Q77.3 Q77.4	Q87.0 Q87.1 Q87.2 Q87.8 Q91 Q92.0 Q92.1 Q92.4 Q92.7			

Supplemental Table 2 Comparison of descriptive statistics between those PICU admissions which did and did not Link to the HES

	Linked		Linkage unsuccessful		x^2	P value
Number	154,667	*99.2*	1316	*0.8*		
Age Category					25.5	<0.001
<1 year	72,170	*99.3*	533	*0.7*		
1-4 years	39,571	*99.1*	347	*0.9*		
5-10 years	20,448	*99.0*	214	*1.0*		
11-15 years	19,003	*99.0*	184	*1.0*		
16+	3,467	*98.9*	38	*1.1*		
missing	8	*100.0*	0	*0.0*		
Sex					0.43	0.51
Male	87,686	*99.2*	726	*0.8*		
Female	66,933	*99.1*	575	*0.9*		
missing	48		15			
Ethnicity					2.6	0.10
Non South Asian	136,670	*99.2*	1,144	*0.8*		
South Asian	17,997	*99.1*	172	*0.9*		
Deprivation Category					148	<0.001
Category 1 (least deprived)	21,421	*99.3*	152	*0.7*		
Category 2	21,816	*98.8*	268	*1.2*		
Category 3	26,341	*98.9*	284	*1.1*		
Category 4	34,498	*99.2*	272	*0.8*		
Category 5 (most deprived)	49,538	*99.5*	230	*0.5*		
missing	1,053	*90.5*	110	*9.5*		
Diagnostic Group (reason for PICU admission)					184	<0.001
Neurological	17,270	*99.0*	181	*1.0*		
Cardiac	44,767	*99.4*	268	*0.6*		
Respiratory	42,230	*99.3*	279	*0.7*		
Oncology	5,190	*98.4*	84	*1.6*		
Infection	8,014	*99.1*	73	*0.9*		
Musculoskeletal	5,736	*98.9*	61	*1.1*		
Gastrointestinal	10,019	*98.9*	112	*1.1*		
Other	8,140	*98.7*	109	*1.3*		
Blood and lymph	1,456	*98.3*	25	*1.7*		
Trauma	4,581	*98.3*	77	*1.7*		
Endocrine/metabolic	3,878	*99.2*	32	*0.8*		
Multisystem	427	*99.5*	2	*0.5*		
Body wall and cavities	2,959	*99.6*	13	*0.4*		
Risk of Mortality (PIM 2)					8.8	0.07
<1%	48,957	*99.2*	415	*0.8*		
1-<5%	74,212	*99.1*	668	*0.9*		
5-<15%	24,727	*99.3*	185	*0.7*		
15-<30%	4,270	*99.4*	25	*0.6*		
>30%	2,501	*99.1*	23	*0.9*		
LOS PICU (days)					10.5	0.11
<1	45,246	*99.1*	426	*0.9*		
1 to <3	49,285	*99.2*	413	*0.8*		

3 to <7	34,122	*99.2*	273	*0.8*		
7 to <14	15,957	*99.3*	120	*0.7*		
14 to <28	6,603	*99.3*	48	*0.7*		
28+	3,412	*99.0*	36	*1.0*		
missing	42		0			
Type of PICU admission					45.5	<0.001
Planned - after surgery	49749	*99.2*	398	*0.79*		
Unplanned after surgery	7688	*99.2*	64	*0.83*		
Planned other	10900	*98.6*	155	*1.40*		
Unplanned	86050	*99.2*	696	*0.80*		
Not known	280		3			
No. PICU admissions					120	<0.001
one admission	77,426	*98.9*	837	*1.1*		
2 admissions	28,850	*99.2*	238	*0.8*		
3 admissions	15,726	*99.4*	90	*0.6*		
4+ admissions	32,665	*99.5*	151	*0.5*		
Year of PICU admission					365	<0.001
2004	12,293	*98.0*	245	*2.0*		
2005	12,326	*98.5*	193	*1.5*		
2006	12,634	*98.8*	150	*1.2*		
2007	13,275	*99.4*	84	*0.6*		
2008	13,462	*99.5*	68	*0.5*		
2009	14,023	*99.3*	100	*0.7*		
2010	14,185	*99.3*	102	*0.7*		
2011	14,006	*99.4*	90	*0.6*		
2012	14,597	*99.2*	111	*0.8*		
2013	14,865	*99.6*	57	*0.4*		
2014	14,973	*99.4*	90	*0.6*		
2015	4,028	*99.4*	26	*0.6*		

Supplemental Table 3a Random Effects Logistic Regression Model for Death in PICU (LLC only)

[n= 88,356, group = 35, wald chi2=5603, sigma_u=0.21, rho=0.02]

	Odds Ratio	**95% Confidence Intervals**		**p-value**
Age Category				
<1 year	REF			
1-4 years	0.85	0.78	0.92	<0.001
5-10 years	0.93	0.84	1.03	0.17
11-15 years	1.03	0.92	1.15	0.66
16+	1.37	1.12	1.67	0.002
Sex				
Male	REF			
Female	1.11	1.04	1.18	0.001
Ethnicity				
Non South Asian	REF			
South Asian	1.30	1.20	1.41	<0.001
Deprivation Category				
Category 1 (least deprived)	REF			
Category 2	1.00	0.88	1.13	0.96
Category 3	1.02	0.90	1.14	0.80
Category 4	1.03	0.92	1.15	0.59
Category 5 (most deprived)	1.03	0.92	1.15	0.60
Diagnostic Group (reason for PICU admission)				
Neurological	1.10	0.97	1.24	0.141
Cardiac	1.16	1.05	1.28	0.003
Respiratory	REF			
Oncology	1.91	1.62	2.25	<0.001
Infection	2.06	1.82	2.35	<0.001
Musculoskeletal	0.74	0.54	1.00	0.05
Gastrointestinal	1.30	1.12	1.51	<0.001
Other	1.07	0.90	1.27	0.43
Blood and lymph	2.54	1.98	3.25	<0.001
Trauma	1.13	0.73	1.74	0.58
Endocrine/metabolic	2.38	2.05	2.76	<0.001
Multisystem	0.61	0.30	1.25	0.18
Body wall and cavities	0.91	0.70	1.17	0.45
Risk of Mortality (PIM 2)				
<1%	REF			
1-<5%	3.86	3.29	4.53	<0.001
5-<15%	8.62	7.28	10.21	<0.001
15-<30%	18.49	15.35	22.29	<0.001
>30%	76.18	62.76	92.48	<0.001
LOS PICU (days)				
<1	1.47	1.33	1.62	<0.001
1 to <3	REF			
3 to <7	0.90	0.81	0.99	0.03
7 to <14	1.16	1.04	1.29	0.01

14 to <28	2.12	1.89	2.37	<0.001
>28	3.96	3.50	4.49	<0.001
Type of PICU admission				
Planned - after surgery	REF			
Unplanned after surgery	1.19	0.98	1.45	0.07
Planned other	1.37	1.17	1.59	<0.001
Unplanned	1.64	1.47	1.83	<0.001
Not known	1.40	0.60	3.29	0.44
Year of Admission	0.97	0.96	0.98	<0.001

Supplemental Table 3b Random Effects Logistic Regression Model for Death in PICU (non LLC only)

[n= 65,132, group = 35, wald chi2=4148, sigma_u=0.28, rho=0.02]

	Odds Ratio	**95% Confidence Intervals**		**p-value**
Age Category				
<1 year	REF			
1-4 years	0.66	0.56	0.77	<0.001
5-10 years	0.96	0.79	1.17	0.69
11-15 years	0.99	0.82	1.20	0.90
16+	1.08	0.60	1.92	0.80
Sex				
Male	REF			
Female	1.06	0.94	1.20	0.31
Ethnicity				
Non South Asian	REF			
South Asian	1.06	0.88	1.27	0.55
Deprivation Category				
Category 1 (least deprived)	REF			
Category 2	1.08	0.85	1.37	0.52
Category 3	1.02	0.81	1.28	0.88
Category 4	1.17	0.94	1.44	0.15
Category 5 (most deprived)	1.17	0.96	1.43	0.13
Diagnostic Group (reason for PICU admission)				
Neurological	2.19	1.79	2.69	<0.001
Cardiac	1.77	1.42	2.21	<0.001
Respiratory	REF			
Oncology	2.12	0.91	4.91	<0.001
Infection	2.05	1.63	2.58	<0.001
Musculoskeletal	0.71	0.24	2.11	0.08
Gastrointestinal	1.82	1.39	2.39	<0.001
Other	1.65	1.25	2.19	0.54
Blood and lymph	1.77	1.00	3.12	<0.001
Trauma	2.37	1.84	3.06	<0.001
Endocrine/metabolic	1.77	1.26	2.50	0.05
Multisystem	1.00			
Body wall and cavities	1.13	0.62	2.05	0.001
Risk of Mortality (PIM 2)				
<1%	REF			
1-<5%	7.14	4.56	11.18	<0.001
5-<15%	34.61	21.95	54.57	<0.001
15-<30%	183.20	113.88	294.69	<0.001
>30%	1530.22	954.72	2452.64	<0.001
LOS PICU (days)				
<1	1.66	1.43	1.93	<0.001
1 to <3	REF			
3 to <7	0.74	0.63	0.88	0.001
7 to <14	0.87	0.70	1.09	0.22
14 to <28	1.56	1.15	2.12	0.004

>28	4.07	2.75	6.02	<0.001
Type of PICU admission				
Planned - after surgery	REF			
Unplanned after surgery	2.04	1.36	3.08	0.001
Planned other	1.25	0.80	1.96	0.321
Unplanned	2.11	1.54	2.88	<0.001
Not known	1.83	0.32	10.33	0.494
Year of Admission	0.95	0.94	0.97	<0.001