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Renal replacement therapy in the critically ill child

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Abstract (290 words)

Objective

Although renal replacement therapy (RRT) is widely used in critically ill children, there have been few comprehensive population based studies of its use. This paper describes RRT use, and associated outcomes, in critically ill children across the United Kingdom (UK) in the largest cohort study of this patient group.

Design

A retrospective observational study using prospectively collected data.

Setting

Data from the Paediatric Intensive Care Audit Network (PICANet) database which collects data on all children admitted to UK Paediatric Intensive Care Units (PICU).

Patients

Children (<16 years) in PICU who received RRT between 1st January 2005 and 31st December 2012 were identified.

Interventions

Individual level data including age, underlying diagnosis, modality (peritoneal dialysis [PD] and continuous extracorporeal techniques [CRRT]), duration of RRT, PICU length of stay and survival were extracted

Measurements and Main results

3825 (2.9%) of 129,809 PICU admissions received RRT in 30 of 33 centres. Volumes of RRT varied considerably from 0 to 8.6% of PICU admissions per unit but volume was not associated with patient survival. Overall survival to PICU discharge (73.8%) was higher than previous reports. Mortality risk was related to: age, with lower risk in older children compared to neonates (Odds Ratio OR 0.6; 95% CI: 0.5-0.8) though mortality did not increase over the age of one year; mode of RRT, with lower risk in

PD than CRRT methodologies (OR 0.7; 0.5-0.9); duration of RRT therapy (OR 1.02 per day; 95% CI: 1.01-1.04); and primary diagnosis, with the lowest survival in liver disease patients (53.9%).

Conclusions

This study describes current RRT use across the UK and associated outcomes. We describe a number of factors associated with outcome, including age, underlying diagnosis, and RRT modality which will need to be factored into future trial design.

Introduction

Renal replacement therapy (RRT) use is well established within the PICU for the management of severe acute kidney injury (AKI), and/or where there is evidence of fluid balance, acid-base and/or metabolic derangement [1]. There is evidence for its usefulness for clearance of toxic metabolites, in particular ammonia, in patients with inborn errors of metabolism and liver failure [2], and RRT may also be used in situations such as severe sepsis or post stem-cell transplantation [3].

A number of recent studies have improved our understanding of AKI in critically ill children. The AWARE (Assessment of Worldwide Acute kidney Injury, Renal Angina and Epidemiology in critically ill children) study investigators, utilising the Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guideline definition and classification of AKI [4], reported an incidence of severe AKI of 11.6% in a population of approximately 5000 children across 32 international sites, and described an association between severity of AKI and mortality. However patients with severe AKI and those treated with RRT are not synonymous; only 1.5% of the above cohort received RRT and 18% (13/73) of the RRT treated group did not meet severe AKI criteria [5].

Continuous methods of RRT are favoured in the unstable critically ill patient. Continuous RRT modalities include peritoneal dialysis (PD) and extracorporeal techniques of continuous veno-venous haemodialysis (CVVHD), continuous veno-venous haemofiltration (CVVH) and continuous veno-venous haemodiafiltration (CVVHDF), which are often collectively termed 'CRRT'. Although the practice of continuous RRT in the critically ill paediatric population is well established, there is a lack of published evidence on optimum use, modality, timing or dose, even in adult populations [6, 7].

Our current understanding of continuous RRT in critically ill children has largely come from a series of publications extracting information from a United States registry of 344 patients from 13 centres treated over a decade ago (2001 to 2005) [8]. Overall

survival was 58%, but only 44% in the infant population, with very poor survival in patients <3kg (25%). Disease specific survival varied from 31% when RRT was undertaken in the context of liver disease to 100% in the setting of drug intoxication. Other publications from the registry have reported a survival disadvantage if 'CRRT' is undertaken in the context of significant fluid overload [9], and have explored circuit survival and importance of vascular access site and size [10], and mode of anticoagulation [11]. Single centre studies with smaller number of continuous RRT patients have been reported including a study of 90 children who received 'CRRT' between 2004 and 2007 with a survival rate of 73% [12] and a recent study of 131 children who received 'CRRT' between 2010 and 2012 with a survival rate of only 46% [13].

In the UK it is mandatory for all PICU's to enter data from every PICU admission prospectively into a national database for audit purposes (Paediatric Intensive Care Audit Network [PICANet]) [14]. Data include patient demographics, severity of illness, diagnostic codes, outcomes, and interventions received during the PICU episode. We set out to describe the characteristics of paediatric patients receiving RRT in UK PICUs and to explore factors affecting outcome.

Methods

Details on every admission over an eight year period (January 1st 2005 to December 31st 2012) of children (under 16 years of age) into all of the 33 UK PICUs were extracted from the PICANet database and those who received RRT were identified.

Throughout this time period continuous RRT was recorded within the PICANet database where one or more episodes of 'haemofiltration' or peritoneal dialysis took place during the PICU admission. The category of 'haemofiltration' is used by PICANet to capture all continuous extracorporeal therapy including haemodialysis and haemodiafiltration and it is not possible to identify which of these 'CRRT' modalities was used. For clarity those patients who were recorded as having 'haemofiltration' will be referred to within our results as the 'CRRT' group. From January 1st 2009 onwards additional data were collected on interventions undertaken each day, including RRT, thereby providing information on the duration of RRT.

The analysis was confined to patients who received one or more forms of continuous RRT, recorded as either 'CRRT' or 'PD'. Children recorded as being treated with *intermittent* haemodialysis were excluded. If cases were identified who received both 'CRRT' and PD these cases were allocated to the 'CRRT' category for analysis.

Standardised mortality ratios (SMRs) with exact binomial confidence limits were calculated by dividing the observed number of deaths by the expected number estimated using the Paediatric Index of Mortality, PIM2 [15] (with coefficients calibrated for the last 3 year patient cohort (2010-2012)) for 'CRRT' and PD across three age groups (neonate [<=28 days], infant [29 days- 365 days], and older child [over 365days-15yrs and 364 days]). Funnel plots were constructed to describe the crude and adjusted mortality rates across PICUs [16]. A logistic regression was carried out to explore the relationship between in-unit mortality and several related factors including age (neonate, infant, older child), type of RRT received ('CRRT', PD), indication / diagnostic category (7 pre-defined categories), PIM2 category (<1%, 1-

5%, 5-15%, 15-30%, 30%+ probability of death) and length of stay (< 7 days, 7-<14 days, 14 days+).

Collection of personally identifiable data without consent has been approved by the Patient Information Advisory Group (now the NHS 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. Anonymised data (cases and units) were extracted with the approval of the PICANet Clinical Advisory and Steering Groups.

Results

3825 (2.9%) of 129,809 admissions to PICU received RRT in 30 out of 33 centres. Of these, 1925 (50.3%) received 'CRRT' 1612 (42.1%) PD, and 288 (7.5%) patients received both 'CRRT' and PD. Over the same period only 186 cases received *intermittent* haemodialysis (Figure 1).

There was considerable variation in the use of continuous RRT across UK PICUs ranging from 0% to 8.6% of all PICU admissions (median 2.3%) (Figure 2a). Figure 2b shows the use of 'CRRT' only (PD excluded), again showing considerable variation from 0% to 4.9% of all PICU admissions (Figure 2b).

Overall, 'CRRT' was used more commonly than PD (57.9% CVVH vs. 42.1% PD) however variation in practice between age groups was noted. PD was used more commonly in the neonatal population (35.7% 'CRRT' vs. 64.3% PD) but 'CRRT' used more commonly in the older age group (80.9% 'CRRT' vs. 19.1% PD) (Table 1).

The most common diagnostic group in those receiving 'CRRT'was sepsis (23.8% of cases), whilst the most common diagnostic group receiving PD was the post cardiac surgery cohort (81.8% of cases) (Tables 2 and 3).

Data on duration of continuous RRT was available for 2139 cases (55.9% of RRT cases). Median duration of therapy was short (2 days [PD], 4 days ['CRRT']) but there was large variation in RRT duration (Tables 2a and 2b). Median duration of 'CRRT' was significantly longer than PD (quantile regression p< 0.001) with 165 (6.6%) cases receiving more than 14 days of therapy (compared to only 28 (1.7%) cases receiving more than 14 days of PD).

Crude mortality for patients receiving continuous RRT was 26.2%, compared to an overall mortality rate across all PICU admissions in the same eight year period of 4.4%. Median per-unit survival to PICU discharge of children receiving any form of continuous RRT was 73.8% (IQR: 64.1%-80.4%) (Figure 3a). In the group of children receiving 'CRRT' this was 66.7% (61.7-73.8 %) (Figure 3b).

PIM2 score was used to adjust for severity of illness at the point of PICU admission, providing an estimate of probability of death for each patient. Standardised mortality ratios were generated for the group receiving continuous RRT. Even accounting for illness severity the group of children who received continuous RRT had a 2-fold excess mortality over that predicted at PICU admission by PIM2 (Overall SMR: 2.05, 95%CI: 1.94, 2.16) (Tables 2 and 3).

A funnel plot of illness severity adjusted mortality did not suggest a relationship between volume of continuous RRT undertaken in each unit and outcome (Figure 3a), even when the analysis was confined to 'CRRT' cases (Figure 3b).

Tables 2 and 3 show outcomes broken down by age group, by modality of continuous RRT, and by diagnostic group.

Survival rates were higher in those receiving PD (82.2%) than those receiving 'CRRT' (67.7%) but this may relate to case selection. PD was used predominantly in neonates and infants after cardiac surgery and the predicted probability of death at PICU admission was significantly higher in patients who received 'CRRT' compared to PD (p<0.05) (Tables 2 and 3).

Older children receiving 'CRRT' had the highest survival rates (70.9% [n=1374]), though the survival rates for 'CRRT' in neonatal (54.7% [n=415]) and infant (70.3% [n=424]) populations are much higher than previously reported. Over the age of one year, survival did not improve with patient age (1-4yrs 73.0% [n=608], 5-10yrs 70.4% [n=368], 11-15yrs 68.1% [n=398]). (Table 1)

Survival was lowest in those receiving 'CRRT' in the setting of liver disease (53.9%) and highest in those with a primary renal disorder (93.3%) (Tables 2 and 3).

A multivariate logistic regression analysis confirmed the statistical significance of a number of the above factors on in-unit mortality (Table 4). The neonatal age group had the highest risk of mortality; the difference between older children and the neonatal group was significant (multivariate OR: 0.6; 95% CI: 0.5-0.8). Those receiving PD had a lower mortality risk than those receiving 'CRRT' (multivariate OR: 0.7; 0.5-0.9). In addition, mortality risk increased with the duration of continuous RRT treatment (multivariate OR: 1.02 per day; 95% CI: 1.01-1.04), and varied significantly with the indication for continuous RRT. As expected PIM2 score predicted an increased risk of mortality (Table 4).

Discussion

Given the large cohort size and the comprehensive nature of data capture from every UK PICU this report provides valuable information on prevalence and outcomes of continuous RRT use in critically ill children. It demonstrates survival rates which are better than those previously reported, particularly in the neonatal and infant populations. This comprehensive description of continuous RRT use across UK PICUs is made possible because of a UK database of all PICU Admissions (PICANet) which has been collecting data since 2003.

A number of factors may have contributed to the apparent improvement in outcomes compared to earlier reports [8, 12, 13]. The number of cases described here is ten-fold larger than previous reports, and represents a more recent cohort suggesting that outcomes may have improved over time. In addition there are almost certainly differences in when and how continuous RRT is initiated between centres. For example the use of high volume 'CRRT' for ammonia clearance in urea cycle disorders or acute liver failure may influence outcomes in these patient groups [2]. It is also possible that continuous RRT is being initiated earlier. For example the knowledge that degree of patient fluid overload is associated with poor outcome [9] may have encouraged clinicians to initiate continuous RRT earlier.

It is also conceivable that the threshold for initiating continuous RRT is lower in the UK. In the recent report by the AWARE study investigators [5], in which US sites predominated, it is noteworthy that only 20.5% (51/249) of children in the highest AKI category (KDIGO 3), defined as a doubling of plasma creatinine or oliguria (< 0.5 mls/kg/hr) for more than 12 hours, received RRT.

Unfortunately a limitation of the current study is that, as a national audit collecting a wide range of data, it does not provide us with details such as plasma creatinine, urine output or degree of fluid overload at initiation of continuous RRT, and therefore we are unable to draw more precise conclusions. In addition as the term 'haemofiltration' is used by PICANet to describe all forms of 'CRRT' (CVVH, CVVHD

and CVVHDF) we are unable to comment on the breakdown of how often the different 'CRRT' modalities were used.

Although the study demonstrates large variation in how often continuous RRT is undertaken across centres, with occasional continuous RRT practice in a number of units, we were not able to demonstrate an effect of volume of continuous RRT performed and patient outcome. This is in contrast to other areas of practice, for example neonatal ECMO, in which a strong association between ECMO volume and lower mortality has been demonstrated [17].

These data provide interesting insights into the uses of 'CRRT' and PD within UK PICU'S. PD is used more commonly in the neonatal and infant population whereas 'CRRT' modalities are used more commonly in the older child. The most obvious explanation for this finding is size and the perception that vascular access and use of 'CRRT 'in small babies is technically difficult and associated with poor circuit and patient survival. This is despite increasing evidence that extracorporeal therapies can be applied safely and effectively in these patient groups [2, 18]. The use of PD over 'CRRT' in cardiac patients, particularly neonates and infants, is likely related to the fact that many of these patients return to the PICU with a PD catheter in situ. This is to allow drainage of any abdominal fluid but it also facilitates commencement of PD if the need for continuous RRT arises, and mitigates the risk of inserting additional vascular access for 'CRRT'. This may also allow clinicians to commence PD relatively 'early', for example to assist in fluid management in the post-operative period.

Patients who received PD had lower PIM2 scores than those who received 'CRRT', which suggests that patients who received 'CRRT' had greater illness severity than those who received PD. This is also reflected in better patient outcomes in the PD group. The use of 'early' PD in the post op cardiac patients may go some way to explaining this but this may also reflect the concept that clinicians see the use of PD and 'CRRT' as a 'stepwise' approach to patient management, and that as insertion of vascular access for 'CRRT' is more invasive and carries greater risk than the insertion of a PD catheter, the patient needs to be sicker, or not adequately managed on PD,

to balance the risk benefit. 288 children (8% of total cohort) were managed with both PD and 'CRRT' during their PICU stay but unfortunately a limitation of the study is that we are unable to provide information on why they changed over from one modality to the other.

Children who receive RRT have increased PICU mortality, over and above that predicted by illness severity at PICU admission (PIM2). There is debate about whether this increased mortality can be improved by introduction of earlier RRT, choice of RRT modality, and 'dose' of RRT but paediatric randomised trials are lacking and adult trials have been inconclusive [7,19,20]. This study will help to inform the feasibility and design of future trials to address these questions.

There are a number of limitations to this report. The dataset collected by PICANET is a general dataset and does not provide granular information. Although PICANet collects data on the use of RRT in an individual patient the haemofiltration classification includes all of the continuous extracorporeal RRT ('CRRT') techniques so we are unable to differentiate how often these different techniques are used. Cases who received more than one form of continuous RRT were allocated to one of the modalities for the purposes of the analysis. We do not have information on the indication for starting continuous RRT or patient status (such as fluid overload or degree of AKI) at the time of initiation. The PICANet database therefore does not provide the very important detail regarding how continuous RRT is administered in each centre, in terms of vascular access and coagulation, specific indications, dose or patient details, such as fluid status, acid base balance or ammonia levels. To gain a more comprehensive understanding of why and how continuous RRT is used an enhanced continuous RRT specific data capture has now been established with the support of PICANet. Another limitation of the study is the use of PIM2 to reflect severity of illness in our patient cohort. PIM2 is calculated on admission data and therefore does not provide information on the patient's status at initiation of continuous RRT, unless continuous RRT was established soon after admission. Finally the study did not collect information on renal outcomes so we are unable to describe the numbers of survivors who required ongoing RRT at PICU discharge.

Future intervention trials are needed to determine if we can lower the significant mortality risk associated with acute kidney injury and multi-organ dysfunction. This study has identified a number of factors, including age, underlying diagnosis, and continuous RRT modality which will need to be factored into trial design and stratification.

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Figure and Table legends

Figure 1 – Case selection.

Figure 2a: Proportion of PICU admissions at each centre undergoing continuous renal replacement therapy (continuous RRT) at any point during their PICU stay and total admissions to each unit during 2005-2012 (displayed in ascending order of admissions).

Figure 2b: Proportion of PICU admissions at each centre undergoing 'CRRT' therapy at any point during their PICU stay and total admissions to each unit during 2005-2012 (displayed in ascending order of admissions).

Figure 3a: Funnel plot of observed crude PICU mortality for units with more than 5 cases. The horizontal solid line represents the overall mortality for children receiving continuous RRT (26%) and each black dot represents one unit. The upper and lower dashed lines represent the 99.9% control limits of the funnel plot.

Figure 3b: Funnel plot of observed crude PICU mortality for units with more than 5 'CRRT' cases. The horizontal line represents the overall mortality for children receiving 'CRRT'(32%) and each black dot represents one unit. The upper and lower dashed lines represent the 99.9% control limits of the funnel plot.

Table 1: Data by age category and outcome (PICU survival) for all patients who received continuous RRT, including a breakdown of 'CRRT' and PD cases.

Table 2: Characteristics of patients who received 'CRRT'.

Table 3: Characteristics of patients who received peritoneal dialysis.

Table 4: Univariate and multivariate logistic regression of in-unit mortality risk for those receiving continuous renal replacement therapy (continuous RRT) at any point during their PICU stay (n=3,825).

Table

Table 1 – Data by age category and outcome (PICU survival) for all patients who received continuous RRT, including a breakdown of 'CRRT' and PD cases.

Number of patients	Neonate			Infant			Older Child		
	Total	Survived	Died	Total	Survived	Died	Total	Survived	Died
Overall Number (%)	1152	803 (69.7)	349 (30.3)	974	763 (78.3)	211 (21.7)	1699	1257 (74.0)	442 (26.0)
'CRRT' Number (%)	415	227 (54.7)	188 (45.3)	424	298 (70.3)	126 (29.7)	1374	973 (70.8)	401 (29.2)
PD Number (%)	737	576 (78.2)	161 (21.8)	550	465 (84.6)	85 (15.5)	325	284 (87.4)	41 (12.6)

('CRRT'- extracorporeal Continuous Renal Replacement Therapies, PD-Peritoneal Dialysis)

Table

Table 2 – Characteristics of patients who received 'CRRT'

Characteristic	Neonate			Infant			Older Child		
	Overall	**Survivors**	**Died**	**Overall**	**Survivors**	**Died**	**Overall**	**Survivors**	**Died**
Age - days median (range)	4 (0-28)	3 (0-26)	5 (0-28)	211 (30-365)	231 (31-365)	149 (30-359)	2143 (366-5839)	2071 (366-5839)	2327 (367-5838)
Weight- KG median (range)	3.0 (2.1-4.4)	3.1 (2.4-4.4)	3.0 (2.1-4.2)	5.8 (2.6-13)	5.6 (2.6-10.5)	6.8 (2.6-13.0)	20.0 (5.0-98.0)	20.0 (5.0-98.0)	19.8 (7.4-78.0)
RRT Duration-days median (range)*	4 (1-101)	4 (1-41)	5 (1-101)	3 (1-36)	2 (1-36)	4 (1-36)	4 (1-167)	4 (1-167)	4.5 (1-64)
LOS-days Median (range)	8.2 (0.1-161.7)	8.2 (0.1-161.7)	8.2 (0.1-109.8)	7.6 (0.1-174.2)	7.2 (0.1-174.2)	8.3 (0.2-65.5)	8.7 (0.1-186.2)	9.0 (0.1-186.2)	7.4 (0.1-161.5)
Indication for RRT [n (%)]									
Liver disease	23 (5.5)	5 (2.2)	18 (9.6)	25 (5.9)	11 (3.7)	14 (11.1)	93 (6.8)	60 (6.2)	33 (8.2)
Renal disease	17 (4.1)	11 (4.8)	6 (3.2)	122 (28.8)	117 (39.3)	5 (4.0)	242 (17.6)	226 (23.2)	16 (4.0)
Cardiac	136 (32.8)	64 (28.2)	72 (38.3)	65 (15.3)	42 (14.1)	23 (18.2)	193 (14.0)	140 (14.4)	53 (13.2)
IEM	91 (21.9)	61 (26.9)	30 (16.0)	8 (1.9)	6 (2.0)	2 (1.6)	38 (2.8)	28 (2.9)	10 (2.5)
Respiratory	59 (14.2)	45 (19.8)	14 (7.5)	49 (11.6)	26 (8.7)	23 (18.3)	138 (10.0)	75 (7.7)	63 (15.7)
Sepsis	44 (10.6)	19 (8.4)	25 (13.3)	109 (25.7)	69 (23.1)	40 (31.8)	374 (27.2)	253 (26.0)	121 (30.2)
Other	45 (10.8)	22 (9.7)	23 (12.2)	46 (10.8)	27 (9.1)	19 (15.1)	296 (21.5)	191 (19.6)	105 (26.2)
PIM2 Category (=estimated probability of death) n (%)									
<1%	13 (13.1)	10 (4.4)	3 (1.6)	51 (12.0)	45 (15.1)	6 (4.8)	97 (7.1)	77 (7.9)	20 (5.0)
1-5%	105 (25.3)	59 (26.0)	46 (24.5)	173 (40.8)	134 (45.0)	39 (31.0)	553 (40.3)	424 (43.6)	129 (32.2)
5-15%	181 (43.6)	111 (48.9)	70 (37.2)	129 (30.4)	88 (29.5)	41 (32.5)	532 (38.7)	376 (38.6)	156 (38.9)
15-30%	73 (17.6)	32 (14.1)	41 (21.8)	43 (10.1)	20 (6.7)	23 (18.2)	102 (7.4)	60 (6.2)	42 (10.5)
30%+	43 (10.4)	15 (6.6)	28 (14.9)	28 (6.6)	11 (3.7)	17 (13.5)	90 (6.6)	36 (3.7)	54 (13.5)
Standardised Mortality Ratio (SMR)									
(SMR)(95% CI)	2.3 (2, 2.5)			2.4 (2.1, 2.8)			2.2 (2.1, 2.4)		

* RRT duration was available for 407 (55.2%) neonates, 298 (54.2%) infants and 187 (57.5%) children
(RRT-renal replacement therapy: LOS-Length of Stay: IEM-Inborn Errors of Metabolism: PIM-Paediatric Index of Mortality)

Table

Table 3 – Characteristics of patients who received peritoneal dialysis

Characteristic	Neonate			Infant			Older Child		
	Overall	**Survivors**	**Died**	**Overall**	**Survivors**	**Died**	**Overall**	**Survivors**	**Died**
Age - days median (range)	6 (0-28)	6 (0-28)	4 (0-27)	114 (29-365)	115 (29-365)	88 (29-350)	932 (366-5839)	880 (366-5839)	1317 (399-5542)
Weight- KG median (range)	3.1 (1.3-4.8)	3.1 (1.7-4.8)	3.0 (1.3-3.8)	4.8 (2.1-10.0)	4.7 (2.2-10.0)	5.1 (2.1-9.0)	13.5 (4.6-46.0)	13.5 (4.6-46.0)	13.5 (7.5-35.0)
RRT Duration- days median (range) *	2 (1, 32)	2 (1, 32)	4 (1, 27)	3 (1, 22)	3 (1, 19)	3 (1, 22)	2 (1, 20)	2 (1, 17)	3 (1, 20)
LOS-days Median (range)	10.0 (0.1-255.9)	9.5 (0.1-100.8)	7.8 (0.1-181.1)	7.8 (0.1-181.4)	7.7 (0.1-181.1)	10.3 (0.2-171.3)	6.9 (0.2-305.8)	6.9 (0.2-305.8)	6.8 (0.3-100.5)
Indication for RRT [n (%)]									
Liver Disease	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.3)	2 (0.6)	2 (4.9)	0 (0.0)
Renal Disease	13 (1.8)	13 (2.3)	0 (0.0)	29 (5.3)	28 (6.0)	1 (1.2)	67 (20.6)	65 (22.9)	2 (4.9)
Cardiac	669 (90.8)	528 (91.7)	141 (87.6)	454 (82.6)	401 (86.2)	53 (62.4)	195 (60.0)	173 (60.9)	22 (53.7)
IEM	4 (0.5)	2 (0.3)	2 (1.2)	4 (0.7)	1 (0.2)	3 (3.5)	0 (0.0)	0 (0.0)	0 (0.0)
Respiratory	2 (0.3)	2 (0.3)	0 (0.0)	18 (3.3)	10 (2.1)	8 (9.4)	15 (4.6)	13 (4.6)	2 (4.9)
Sepsis	21 (2.9)	11 (1.9)	10 (6.2)	29 (5.3)	16 (3.4)	13 (15.3)	18 (5.5)	12 (4.2)	6 (14.6)
Other	28 (3.8)	20 (3.5)	8 (5.0)	14 (2.6)	9 (1.9)	5 (5.9)	28 (8.6)	21 (7.4)	7 (17.1)
PIM2 Category (estimated probability of death) n (%)									
<1%	39 (5.3)	37 (6.4)	2 (1.2)	104 (18.9)	98 (21.1)	6 (7.1)	56 (17.2)	53 (18.7)	3 (7.3)
1-5%	375 (50.9)	324 (56.3)	51 (31.7)	346 (62.9)	306 (65.8)	40 (47.1)	191 (58.8)	177 (62.3)	14 (34.1)
5-15%	221 (30.0)	155 (26.9)	66 (41.0)	67 (12.2)	43 (9.2)	24 (28.2)	58 (17.8)	46 (16.2)	12 (29.3)
15-30%	60 (8.1)	39 (6.8)	21 (13.0)	19 (3.5)	12 (2.6)	7 (8.2)	14 (4.3)	5 (1.8)	9 (22.0)
30%+	42 (5.7)	21 (3.7)	21 (13.0)	14 (2.6)	6 (1.3)	8 (9.4)	6 (1.8)	3 (1.1)	3 (7.3)
Standardised Mortality Ratio									
(SMR)(95% CI)	1.5 (1.3, 1.7)			2.1 (1.7, 2.6)			1.5 (1.1, 2)		

* RRT duration was available for 407 (55.2%) neonates, 298 (54.2%) infants and 187 (57.5%) children

(RRT-renal replacement therapy: LOS-Length of Stay: IEM-Inborn Errors of Metabolism: PIM-Paediatric Index of Mortality)

Table

Table 4: Univariate and multivariate logistic regression of in-unit mortality risk for those receiving continuous renal replacement therapy (continuous RRT) at any point during their PICU stay (n=3,825)

Risk Factor	N	%	Univariate			Multivariate		
			Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value
Age								
Neonate	1,152	*30.1*	1.0	Ref		1.0	Ref	
Infant	974	*25.5*	0.6	0.5-0.8	<0.001	0.9	0.6-1.2	0.346
Older child	1,699	*44.4*	0.8	0.7-1.0	0.012	0.6	0.5-0.8	0.001
Type of RRT								
'CRRT'	2,213	*57.9*	1.0	Ref		1.0	Ref	
Peritoneal Dialysis	1,612	*42.1*	0.5	0.4-0.5	<0.001	0.7	0.5-0.9	0.005
Indication for RRT*								
Liver disease	145	*3.8*	3.4	2.4-4.8	<0.001	1.7	1.0-2.8	0.036
Renal Disease	407	*10.6*	0.2	0.2-0.4	<0.001	0.2	0.1-0.3	<0.001
Cardiac	1,712	*44.8*	1.0	Ref		1.0	Ref	
IEM	145	*3.8*	1.8	1.2-2.6	0.002	0.9	0.5-1.5	0.635
Respiratory	281	*7.4*	2.4	1.8-3.1	<0.001	1.5	1.0-2.4	0.043
Sepsis	595	*15.6*	2.1	1.7-2.6	<0.001	1.3	0.9-1.9	0.196
Other	540	*14.1*	1.7	1.4-2.2	<0.001	1.3	0.9-1.9	0.204
PIM2 Category								
<1%	360	*9.4*	1.0	Ref		1.0	Ref	
1-5%	1,743	*45.6*	1.8	1.3-2.5	0.001	1.5	0.9-2.5	0.085
5-15%	1,188	*31.1*	3.6	2.5-5.1	<0.001	2.3	1.4-3.8	0.001
15-30%	311	*8.1*	6.8	4.6-10.1	<0.001	4.7	2.7-8.2	<0.001
30%+	223	*5.8*	11.4	7.5-17.4	<0.001	7.9	4.4-14.3	<0.001
Length of RRT								
Per day of RRT			1.03	1.02-1.05	<0.001	1.02	1.01-1.04	<0.001

* Cardiac was chosen as the reference category as contained the largest number of patients.

Figure

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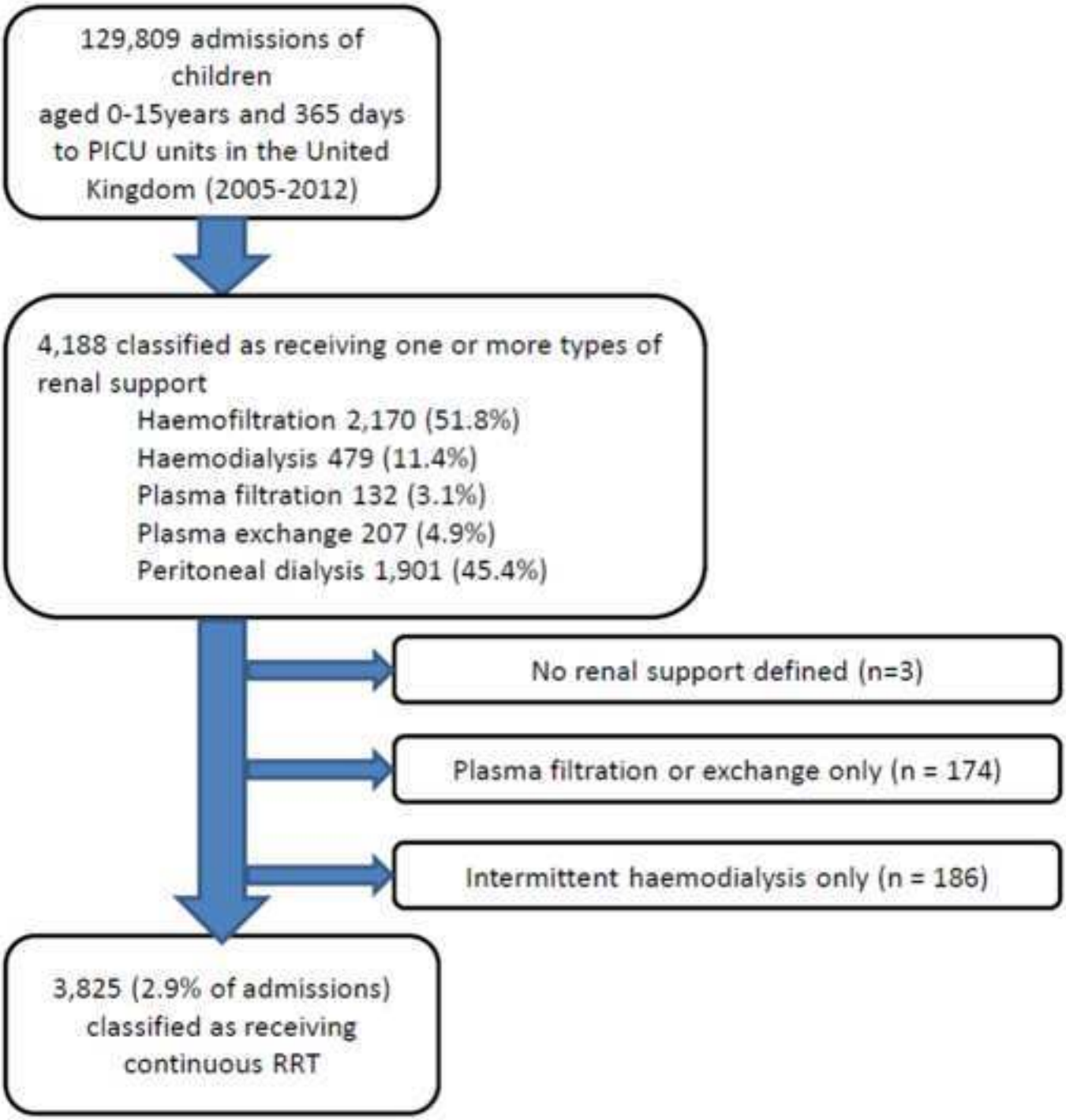

Figure

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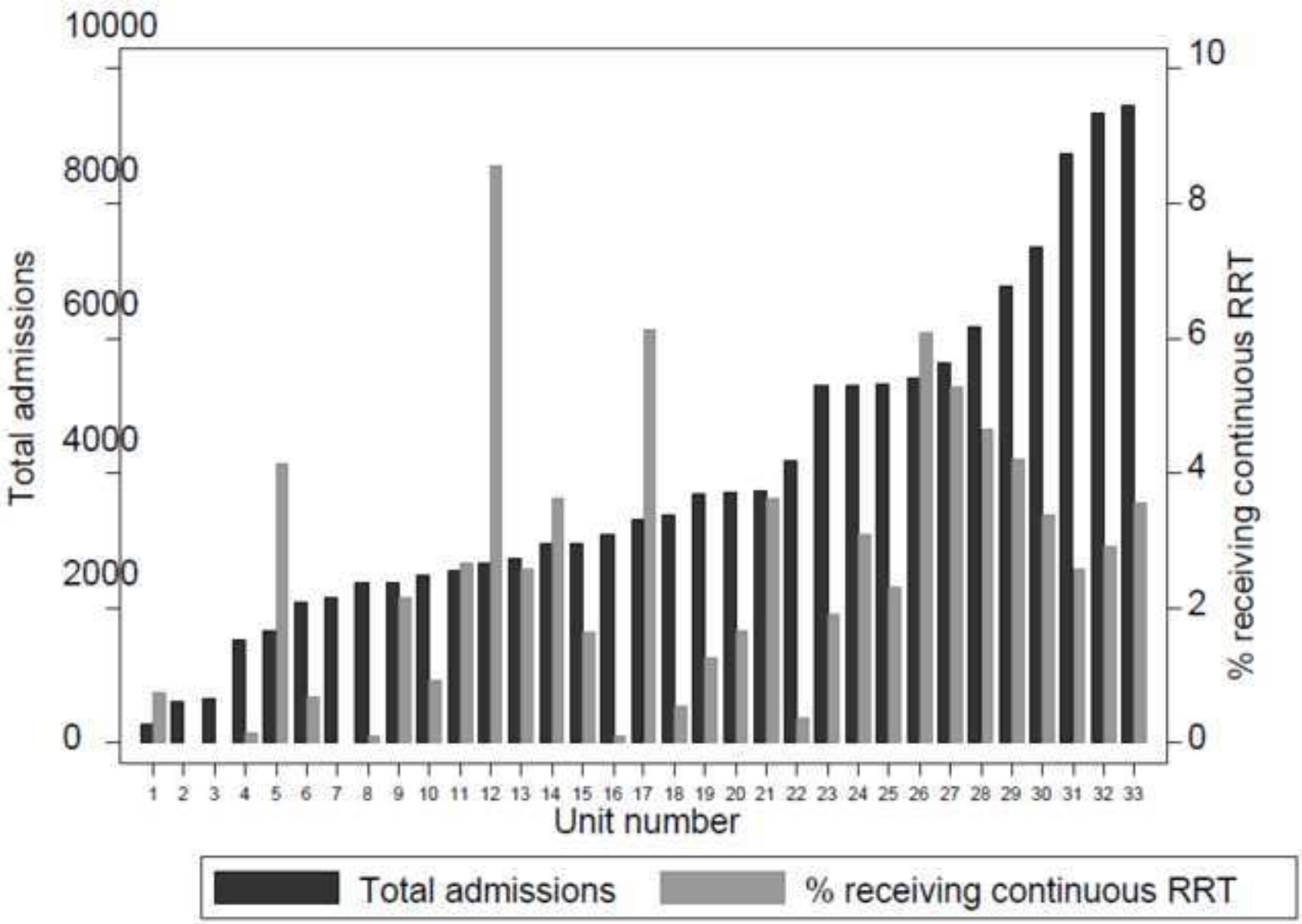

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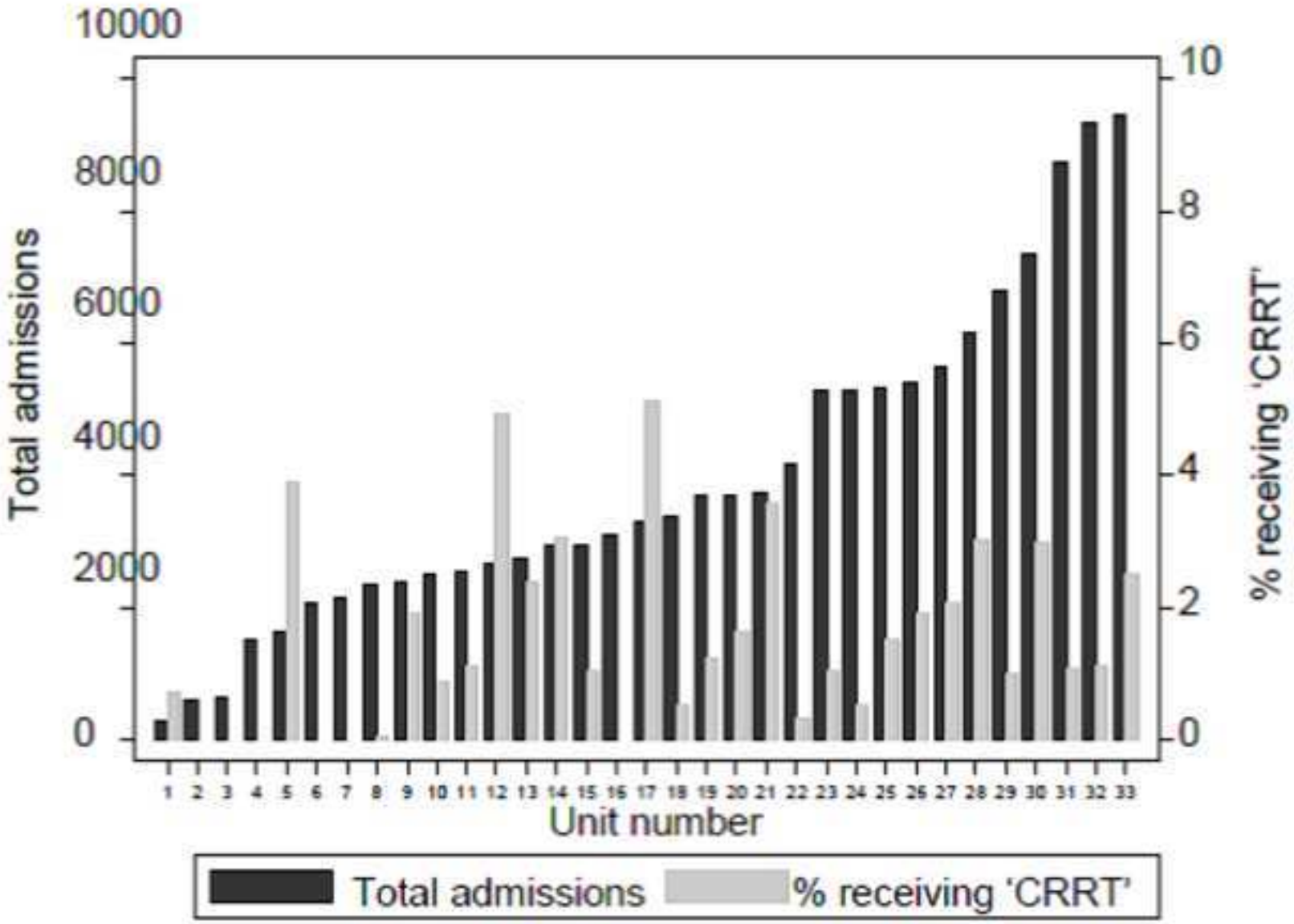

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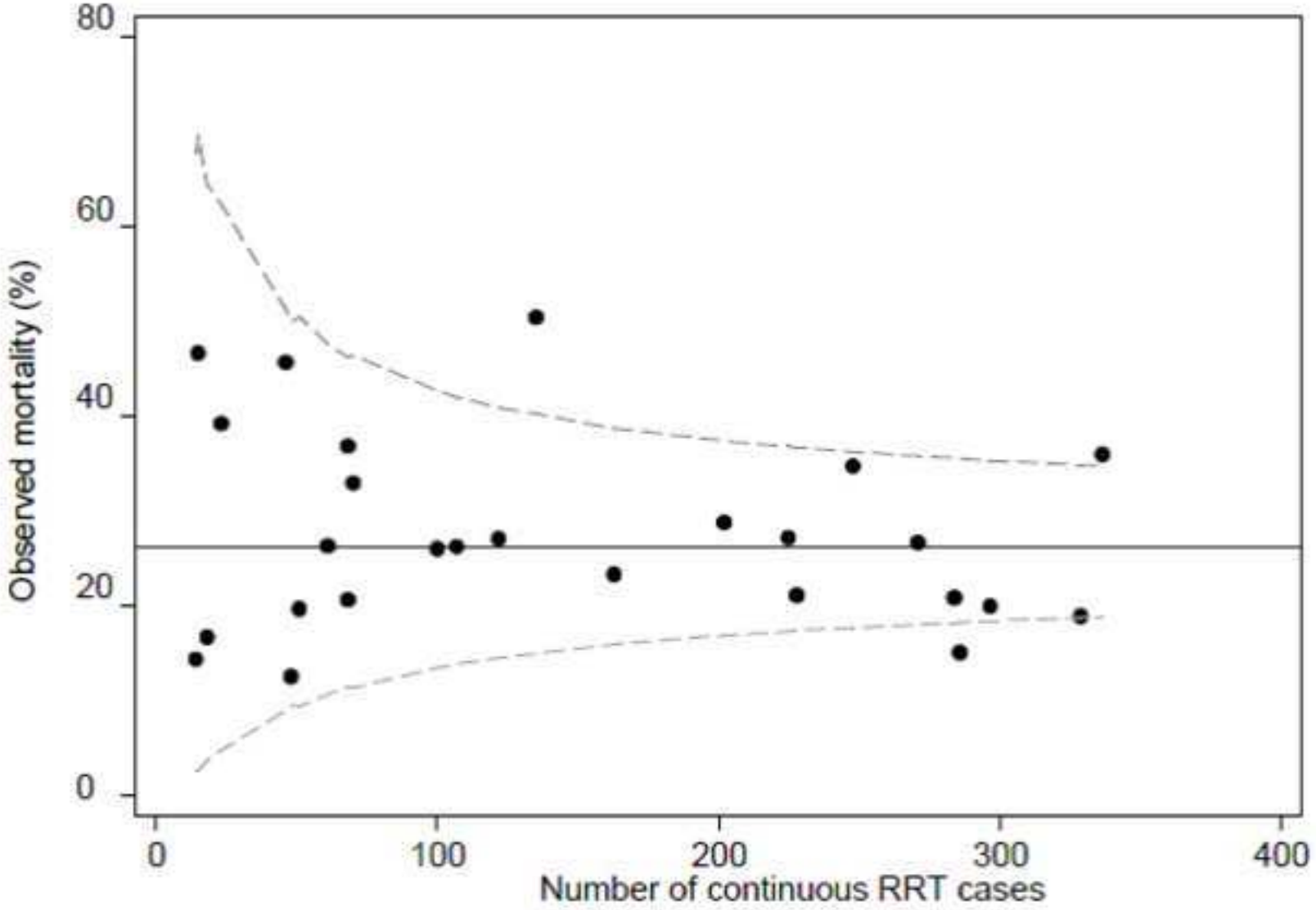

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