UK Renal Registry 17th Annual Report: Chapter 4 Demography of the UK Paediatric Renal Replacement Therapy Population in 2013

Rishi Pruthi[a], Alexander J Hamilton[a], Catherine O'Brien[b], Anna Casula[a], Fiona Braddon[a], Carol Inward[c], Malcolm Lewis[d], Heather Maxwell[e], Jelena Stojanovic[f], Yincent Tse[g], Manish D Sinha[f]

[a]UK Renal Registry, Bristol, UK; [b]Birmingham Children's Hospital, Birmingham, UK; [c]Bristol Royal Hospital for Children, Bristol, UK; [d]Royal Manchester Children's Hospital, Manchester, UK; [e]Royal Hospital for Sick Children, Glasgow, UK; [f]Evelina London Children's Hospital, London, UK; [g]Great North Children's Hospital, Newcastle Upon Tyne, UK

Key Words

Aetiology · Children · Demography · End stage renal disease · Established renal failure · Incidence · Prevalence · Pre-emptive transplantation · Renal replacement therapy · Survival

Summary

- A total of 891 children and young people under 18 years with established renal failure (ERF) were receiving treatment at paediatric nephrology centres in 2013.
- At the census date (31st December 2013), 80.2% of prevalent paediatric patients aged <18 years had a functioning kidney transplant, 11.7% were receiving haemodialysis (HD) and 8.1% were receiving peritoneal dialysis (PD).
- In patients aged <16 years the prevalence of ERF was 58.2 per million age related population (pmarp) and the incidence 9.3 pmarp, in 2013.
- The most common diagnosis was renal dysplasia ± reflux, present in 34.2% of prevalent paediatric patients aged <16 years in 2013.
- About a third of patients had one or more reported comorbidities at onset of renal replacement therapy (RRT).
- The improvement in rates of pre-emptive transplantation for those referred early has remained consistent over the last 10 years at 36.3%, compared to 26.9% in 1999–2003.
- At transfer to adult services, 85.2% of patients had a functioning kidney transplant.
- Survival during childhood amongst children commencing RRT was the lowest in both those aged less than two years old with a hazard ratio of 5.0 (confidence interval 2.8–8.8), and in those receiving dialysis compared to having a functioning transplant with a hazard ratio of 7.1 (confidence interval 4.7–11.7).

Introduction

Established renal failure requiring renal replacement therapy is a significant cause of long term morbidity and mortality during childhood, with specialist care being provided in 13 paediatric nephrology centres in the UK. All centres are equipped to provide peritoneal dialysis and haemodialysis, with ten centres also undertaking kidney transplantation for children. In the UK in 2012, the prevalence rate of treated ERF in children aged under 16 years was 56.7 and the incidence rate was 9.0 per million age related population [1].

The objectives of this report are:

(i) To describe the UK prevalence, incidence, causes of ERF and modality of treatment of children on RRT on 31st December 2013
(ii) To describe trends in (i) over the past 15 years, and
(iii) To describe pre-emptive transplantation rates and survival of children on RRT aged <16 years old in the UK.

Methods

Data collection was performed by all 13 paediatric nephrology centres managing children on RRT in the UK in 2013. Data submission to the UK Renal Registry (UKRR) in previous years has been electronic in most cases with diminishing proportions of paper-based returns over the past few years. All data items are then checked, validated and manually entered into the current paediatric UKRR database.

In this report, patient groups are described as: (i) 'prevalent' group: patients who were receiving RRT on the 31st December 2013; (ii) 'incident' group: patients who started RRT between 1st January and 31st December 2013; and (iii) '5 year' groups: patients who started RRT in the periods of 1999–2003, 2004–2008 and 2009–2013.

The populations used to calculate the incidence and prevalence rates were obtained from the Office for National Statistics (ONS) [2]. The mid-2013 population estimate produced by the ONS, based on the 2011 Census, was used for calculating the 2013 incident and prevalent group rates; the 2001 Census data was used for the 1999–2003 '5 year' group, the 2006 data for the 2004–2008 '5 year' group and the 2011 data for the 2009–2013 '5 year' group.

Infants under the age of three months and 'late presenters' (defined as children commencing dialysis within three months following first review by a paediatric nephrologist) were excluded from analyses when calculating pre-emptive transplantation rates. For survival analysis, only patients starting RRT between 1st January 1999 and 31st December 2012 were included to ensure a minimum of one year follow up at the census date (31st December 2013), and were followed up to a maximum age of 16 years.

Statistical analyses

Statistical analyses were performed using SAS 9.3, with group analyses using the Chi-square test and median analyses using the Kruskal-Wallis test. A Cox regression model was used in calculating hazard ratios for patient survival, adjusting for gender, age at start of RRT, and RRT modality as a time dependent variable. Survival probabilities were calculated using univariate Kaplan Meier curves.

Results

Accuracy and completeness of data returns

All centres submitted data electronically to the UKRR in 2013. The data returns now show near 100% data completeness being achieved by all centres for a range of data items including gender, ethnicity, treatment modality and age at start of RRT. Data completeness for other core items was similar to previous reports [1] and is shown in table 4.1.

The UK paediatric prevalent ERF population in 2013

A total of 891 children and young people under 18 years with ERF were receiving treatment at paediatric nephrology centres in 2013 (table 4.1). At the census date, 80.2% had a functioning kidney transplant, 11.7% were receiving HD and 8.1% were receiving PD (table 4.4).

Patients aged 16–18 years may receive their medical care either in a paediatric or in an adult nephrology centre. Adult renal centres report RRT patients over the age of 18 years to the UKRR. As data were incomplete for the 16–18 year old patients, they have been excluded from the majority of subsequent analyses (particularly when describing incidence and prevalence rates).

There were 702 children under 16 years of age receiving RRT in the UK in 2013. Table 4.2 shows the number of patients receiving RRT and rate of RRT pmarp by age group and gender. The prevalence of RRT increased with age and was higher in males across all age groups with an overall male to female prevalence ratio of 1.5 : 1. The reported prevalence rate in under 16 year olds was 58.2 pmarp.

Table 4.3 shows the ethnic origin of current RRT patients and their prevalence rates. Children from ethnic minorities displayed higher prevalent rates of RRT when compared with White children, with South Asian children displaying the highest rates.

Table 4.1. Data completeness for paediatric prevalent ERF population in 2013

		Percentage completeness				
Centre	*N*	First seen date	Height at RRT start	Weight at RRT start	Creatinine at RRT start	Primary renal diagnosis
Blfst_P*	35	94.3	85.7	88.6	94.3	100.0
Bham_P*	96	97.9	94.8	95.8	94.8	86.5
Brstl_P*	54	100.0	98.2	100.0	100.0	100.0
Cardf_P	25	100.0	96.0	96.0	96.0	100.0
Glasg_P*	50	96.0	90.0	94.0	96.0	100.0
L Eve_P*	98	100.0	68.4	75.5	76.5	100.0
L GOSH_P*	189	97.4	86.8	94.7	93.1	100.0
Leeds_P*	85	98.8	87.1	97.7	97.7	98.8
Livpl_P	39	97.4	79.5	84.6	94.9	97.4
Manch_P*	76	94.7	90.8	96.1	96.1	100.0
Newc_P*	33	100.0	90.9	90.9	90.9	100.0
Nottm_P*	86	97.7	68.6	81.4	98.8	98.8
Soton_P	25	100.0	76.0	76.0	92.0	96.0
UK	**891**	**97.9**	**84.9**	**90.8**	**93.4**	**98.1**

*Denotes centre undertaking kidney transplantation for children

Table 4.2. The UK paediatric prevalent ERF population <16 years old in 2013, by age group and gender

	All patients		Males		Females		M:F
Age group	*N*	pmarp	*N*	pmarp	*N*	pmarp	rate ratio
0–<2 years	23	14.2	16	19.3	7	8.9	2.2
2–<4 years	48	29.8	37	44.9	11	14.0	3.2
4–<8 years	150	48.2	89	55.8	61	40.1	1.4
8–<12 years	201	71.5	125	86.8	76	55.4	1.6
12–<16 years	280	96.2	158	106.0	122	85.9	1.2
Under 16 years	**702**	**58.2**	**425**	**68.8**	**277**	**47.1**	**1.5**

pmarp – per million age related population

Table 4.3. The UK paediatric prevalent ERF population <16 years old by age and ethnic group in 2013[a]

	White		South Asian		Black		Other[b]
Age group	*N*	pmarp	*N*	pmarp	*N*	pmarp	*N*
0–<4 years	45	17.4	9	42.7	2	23.7	9
4–<8 years	94	39.3	30	153.8	4	51.3	17
8–<12 years	144	56.3	33	158.3	8	95.9	7
12–<16 years	201	74.6	41	186.7	9	102.5	18
Under 16 years	**484**	**47.3**	**113**	**135.5**	**23**	**68.9**	**51**

pmarp – per million age related population
[a]ethnicity data missing for 31 children not included in this table
[b]pmarp not expressed for group 'Other', as heterogeneous group

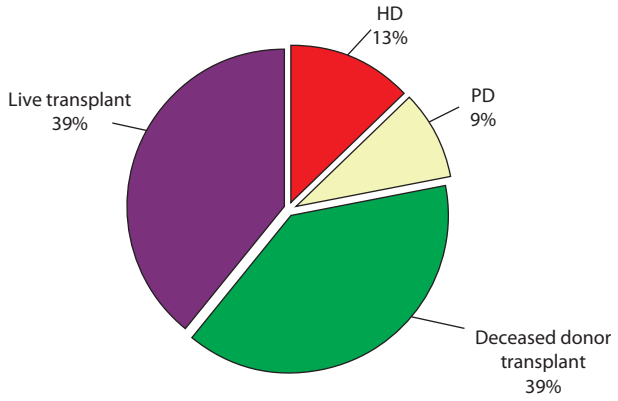

Fig. 4.1. RRT treatment used by prevalent paediatric patients <16 years old in 2013

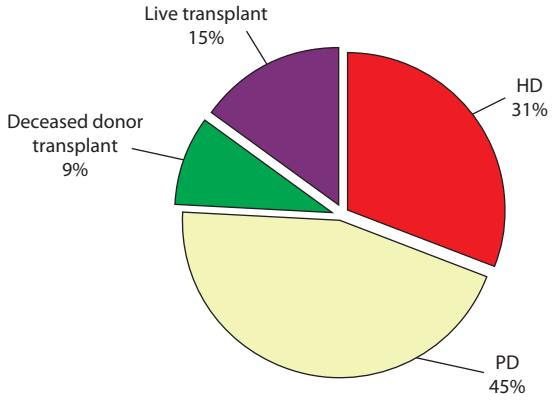

Fig. 4.2. Treatment modality at start of RRT in prevalent paediatric patients <16 years old in 2013

Modality of treatment

Current treatment modality in the prevalent paediatric population less than 16 years old in 2013 is displayed in figure 4.1. Of the 78% with a functioning transplant, 50% received a deceased donor transplant and 50% a living donor transplant.

The treatment modality in use at the start of RRT is displayed in figure 4.2. This shows that 45% of patients were treated with PD at the start of RRT whilst 31% of patients were treated with HD. Of children under 16, 24% were reported to have received a pre-emptive transplant.

Further treatment modality analysis by age is shown in table 4.4 which demonstrates that in the under two year old age group one child received a live transplant and that almost similar proportions of patients were being treated with PD (52.2%) and HD (43.5%). This contrasts with older children from the age of 8 to <16 years where approximately 85% had a functioning graft and twice the number of patients were on HD compared to PD. Subsequent analysis of RRT modality by gender and ethnicity showed no difference. However, as absolute sub-group numbers are small, caution is needed in conducting any comparative analyses.

Cause of ERF

Table 4.5 shows the diagnostic categories for the prevalent ERF population under 16 years in 2013 and figure 4.3 displays the percentage of patients in each diagnostic category for incident and prevalent cohorts. In comparison to previous years, (0.7% in 2012 [1] and 0.4% in 2011 [3]) 2.1% of children had a missing diagnosis in 2013.

Of the 702 patients, renal dysplasia ± reflux remained the commonest condition causing ERF (34%), whilst there were no documented patients with drug nephrotoxicity.

Table 4.4. Current treatment modality by age in the prevalent paediatric ERF population in 2013

		Current treatment							
		HD		PD		Live transplant		Deceased donor transplant	
Age group	Total	*N*	%	*N*	%	*N*	%	*N*	%
0–<2 years	23	10	43.5	12	52.2	1	4.3	0	0.0
2–<4 years	48	13	27.1	15	31.3	16	33.3	4	8.3
4–<8 years	150	15	10.0	12	8.0	79	52.7	44	29.3
8–<12 years	201	20	10.0	11	5.5	79	39.3	91	45.3
12–<16 years	280	31	11.1	13	4.6	102	36.4	134	47.9
16–<18 years	189	15	7.9	9	4.8	71	37.6	94	49.7
Under 16 years	**702**	**89**	**12.7**	**63**	**9.0**	**277**	**39.5**	**273**	**38.9**
Under 18 years	**891**	**104**	**11.7**	**72**	**8.1**	**348**	**39.1**	**367**	**41.2**

Table 4.5. Number, percentage and gender by primary renal disease as cause of ERF in the prevalent paediatric ERF population under 16 years in 2013*

Diagnostic group	*N*	%	Male	Female	M:F ratio
Renal dysplasia ± reflux	240	34.2	147	93	1.6
Obstructive uropathy	128	18.2	121	7	17.3
Glomerular disease	74	10.5	32	42	0.8
Congenital nephrotic syndrome	68	9.7	37	31	1.2
Tubulo-interstitial diseases	46	6.6	19	27	0.7
Renovascular disease	32	4.6	19	13	1.5
Polycystic kidney disease	31	4.4	11	20	0.6
Metabolic	27	3.8	14	13	1.1
Uncertain aetiology	25	3.6	11	14	0.8
Malignancy & associated disease	16	2.3	5	11	0.5
Missing	15	2.1	9	6	1.5
Total	**702**	**100**	**425**	**277**	**1.5**

*In 2013 there were no patients with ERF secondary to 'drug nephrotoxicity'

As for associated comorbidities at the onset of RRT, table 4.6 shows that congenital abnormalities were the commonest, reported in 9.0% of patients, followed by developmental delay at 8.3%. Overall 67.7% of patients had no registered comorbidities, with 21.8% having one comorbidity listed, and 10.5% having two or more comorbidities. Centre analysis showed significant variation in reporting of registered comorbidities with some centres, e.g. Cardiff (89%), Birmingham (83%), London GOSH (82%), Glasgow (80%) and London Evelina (80%) reporting no comorbidity in the majority of their patients, as compared to other centres which reported no comorbidity in a smaller proportion of patients, e.g. Bristol (36%), Manchester (43%) and Belfast (43%). Causes of the variation in reporting need to be understood as there may be genuine differences between centres in willingness to accept patients with comorbidity onto the RRT programme.

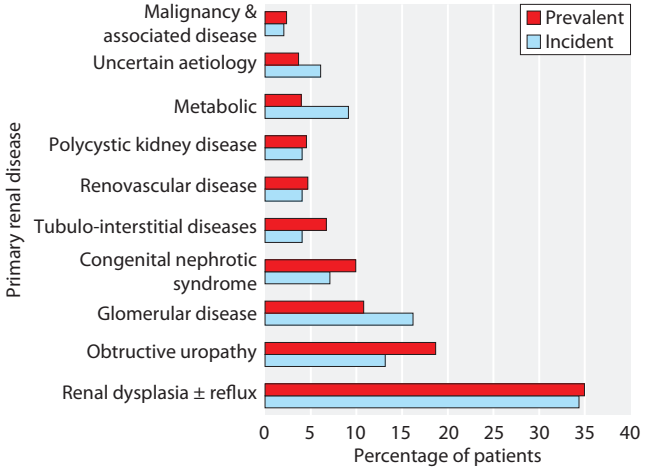

Fig. 4.3. Primary renal disease percentage in incident and prevalent paediatric ERF patients <16 years old in 2013 for whom a causative diagnosis was reported

The UK incident paediatric ERF population in 2013

There were 124 patients under 18 years of age who commenced RRT at paediatric renal centres in 2013. As previously, the following analyses are restricted to the 112 patients who were under 16 years of age.

Table 4.6. Frequency of registered comorbidities at onset of RRT in prevalent paediatric patients aged <16 years with ERF in 2013

Comorbidity	*N*	Percentage of all RRT patients
Congenital abnormality	63	9.0
Developmental delay	58	8.3
Syndromic diagnosis	55	7.8
Prematurity	48	6.8
Consanguinity	29	4.1
Chromosomal abnormality	14	2.0
Family member with ERF	14	2.0
Congenital heart disease	11	1.6
Liver disease	11	1.6
Cerebral palsy	8	1.1
Malignancy	6	0.9
Psychological disorder	5	0.7
Neural tube defect	4	0.6
Diabetes	1	0.1
No reported comorbidity	475	67.7
One reported comorbidity	153	21.8
Two or more comorbidities	74	10.5

Table 4.7. The incident paediatric ERF population <16 years old in the UK in 2013, by age group and gender

	All patients		Male		Female		
Age group	*N*	pmarp	*N*	pmarp	*N*	pmarp	M:F ratio
0–<2 years	19	11.8	13	15.7	6	7.6	2.1
2–<4 years	17	10.6	11	13.4	6	7.6	1.7
4–<8 years	14	4.5	4	2.5	10	6.6	0.4
8–<12 years	31	11.0	20	13.9	11	8.0	1.7
12–<16 years	31	10.7	12	8.1	19	13.4	0.6
Under 16 years	**112**	**9.3**	**60**	**9.7**	**52**	**8.8**	**1.1**

pmarp – per million age related population

The incidence rate of RRT was 9.3 pmarp in 2013. Patients commencing RRT in 2013 are displayed by age and gender in table 4.7.

Table 4.8 shows that the reported incidence of RRT has remained between 9.2 and 10.0 pmarp since 1999, with the highest incidence rates seen in both the youngest and oldest age groups.

Trends in ERF demographics

There were 1,681 children under 16 years of age who had received RRT in the UK over the 15 year period between 1999 and 2013. Analysis of ERF demographics for children less than 16 years of age over this period included 546 patients reported to the paediatric registry in 1999–2003, 575 in 2004–2008 and 560 in 2009–2013. In table 4.9, comparing the current 5-year period with the two previous 5-year periods has shown a sustained increase in the number of younger children aged 0–<8 years starting RRT. Conversely there has been a sustained reduction in numbers of older children aged 8–<16 years. The percentage of children on RRT who were from a South Asian ethnic background also increased during this period, although table 4.10 shows that the level of missing ethnicity data has recently increased considerably. Table 4.11 demonstrates that the reported patient population at most paediatric renal centres has fluctuated in size since 1999–2003.

Table 4.12 shows the number and percentage of children receiving RRT with each of the major reported comorbidities over the last 15 years. Syndromic diagnoses (8.2%), developmental delay (7.7%) and congenital abnormalities (7.3%) continued to be the most common reported comorbidities in 2009–2013. There has been a noticeable reported decrease in frequencies of consanguinity, family history of ERF and chromosomal

Table 4.8. Reported average incident rate by age group in 5-year time periods of children under 16 years of age commencing RRT

	Per million age related population		
Age group	1999–2003	2004–2008	2009–2013
0–<2 years	11.0	14.1	12.4
2–<4 years	6.2	6.5	8.4
4–<8 years	5.3	6.8	6.3
8–<12 years	9.1	8.3	9.0
12–<16 years	13.6	14.0	12.7
Under 16 years	**9.2**	**10.0**	**9.6**

Table 4.9. Number and percentage of children <16 years old who commenced RRT by age group and 5-year period at start of RRT

	1999–2003		2004–2008		2009–2013		1999–2013
Age group	*N*	%	*N*	%	*N*	%	% change
0–<2 years	74	13.6	102	17.7	98	17.5	3.9
2–<4 years	44	8.1	45	7.8	65	11.6	3.5
4–<8 years	78	14.3	92	16.0	90	16.1	1.8
8–<12 years	141	25.8	120	20.9	122	21.8	−4.0
12–<16 years	209	38.3	216	37.6	185	33.0	−5.2
Under 16 years	**546**		**575**		**560**		

Table 4.10. Number and percentage of children under 16 years who commenced RRT, by ethnicity and 5-year period of starting RRT*

	1999–2003		2004–2008		2009–2013		1999–2013
Ethnic group	*N*	%	*N*	%	*N*	%	% change
White	424	78.1	433	76.4	368	70.1	−8.0
South Asian	84	15.5	87	15.3	96	18.3	2.8
Black	14	2.6	23	4.1	17	3.2	0.7
Other	21	3.9	24	4.2	44	8.4	4.5
Under 16 years	**543**		**567**		**525**		

*Three children in 1999–2003, eight in 2004–2008 and thirty five in 2009–2013 with no ethnicity recorded are excluded from this table

Table 4.11. Number and percentage of children under 16 years by renal centre and 5-year period of starting RRT*

	1999–2003		2004–2008		2009–2013		1999–2013
Centre	*N*	%	*N*	%	*N*	%	% change
Blfst_P	18	3.3	14	2.4	25	4.5	1.2
Bham_P	52	9.5	63	11.0	63	11.3	1.7
Brstl_P	38	7.0	36	6.3	31	5.5	−1.4
Cardf_P	15	2.8	20	3.5	17	3.0	0.3
Glasg_P	36	6.6	46	8.0	36	6.4	−0.2
L Eve_P	56	10.3	55	9.6	59	10.5	0.3
L GOSH_P	91	16.7	114	19.8	118	21.1	4.4
Leeds_P	47	8.6	60	10.4	44	7.9	−0.8
Livpl_P	26	4.8	27	4.7	16	2.9	−1.9
Manch_P	60	11.0	44	7.7	61	10.9	−0.1
Newc_P	29	5.3	28	4.9	17	3.0	−2.3
Nottm_P	53	9.7	56	9.7	53	9.5	−0.3
Soton_P	24	4.4	12	2.1	20	3.6	−0.8
Total <16	**545**		**575**		**560**		

*One child in 1999–2003 with an unknown centre at start of RRT was excluded from this table

Table 4.12. Trends in comorbidity frequency at the start of RRT in the paediatric population under 16 years by 5-year period

	1999–2003		2004–2008		2009–2013		1999–2013
Comorbidity	*N*	%	*N*	%	*N*	%	% change
Syndromic diagnosis	37	6.8	50	8.7	46	8.2	1.4
Developmental delay	42	7.7	45	7.8	43	7.7	0.0
Congenital abnormality	42	7.7	51	8.9	41	7.3	−0.4
Prematurity	27	4.9	30	5.2	31	5.5	0.6
Consanguinity	28	5.1	17	3.0	19	3.4	−1.7
Family member with ERF	23	4.2	15	2.6	11	2.0	−2.2
Congenital heart disease	12	2.2	18	3.1	9	1.6	−0.6
Psychological disorder	12	2.2	4	0.7	9	1.6	−0.6
Liver disease	5	0.9	13	2.3	7	1.3	0.3
Cerebral palsy	7	1.3	13	2.3	6	1.1	−0.2
Neural tube defect	1	0.2	5	0.9	6	1.1	0.9
Chromosomal abnormality	19	3.5	17	3.0	4	0.7	−2.8
Malignancy	7	1.3	4	0.7	4	0.7	−0.6
Diabetes	4	0.7	4	0.7	1	0.2	−0.6
No reported comorbidity	360	65.9	383	66.6	399	71.3	5.3
One reported comorbidity	130	23.8	130	22.6	108	19.3	−4.5
Two or more comorbidities	56	10.3	62	10.8	53	9.5	−0.8

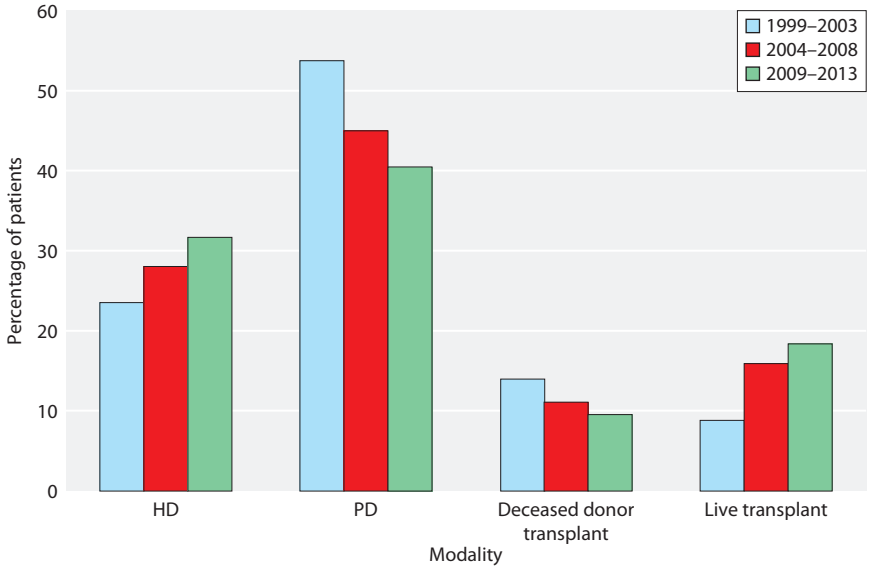

Fig. 4.4. Treatment modality at start of RRT for incident paediatric patients <16 years old by 5-year time period

abnormalities. Overall there is a trend towards the reporting of no comorbidities in children receiving RRT over the last 15 years and it should be clarified whether this is truly due to identifying fewer comorbidities or a result of underreporting.

As for changes in modality at the start of RRT, figure 4.4 shows that the percentage of children who were using PD at the start of RRT has fallen from 53.7% in 1999–2003 to 40.5% in 2009–2013, whilst the percentage commencing RRT on HD increased from 23.5% in 1999–2003 to 31.7% in 2009–2013. During this period the overall percentage receiving a transplant at the start of RRT rose from 22.8% to 27.9%, with an increase in living donation from 8.8% to 18.4%, and a corresponding fall in deceased donor transplantation from 14.0% to 9.5% for the same time period.

Table 4.13 shows the diagnostic categories for 540 of the 546 (98.9%) patients in 1999–2003, for 566 of the 575 (98.4%) patients in 2004–2008 and 540 of the 560 (96.4%) patients in 2009–2013 aged <16 years for whom a causative diagnosis was reported. Overall there has been an increase in the percentage of children receiving RRT with renal dysplasia ± reflux and obstructive uropathy whilst the frequency of glomerular disease has fallen markedly. In addition, numbers with uncertain aetiology have increased whilst those with malignancy

Table 4.13. Number and percentage of children under 16 years for whom a primary renal diagnosis had been reported as a cause of ERF, by 5-year time period and observed change in proportion of patients in each diagnostic group*

	1999–2003		2004–2008		2009–2013		1999–2013
Primary renal diagnosis	*N*	%	*N*	%	*N*	%	% change
Renal dysplasia ± reflux	157	29.1	191	33.7	182	33.7	4.6
Obstructive uropathy	80	14.8	75	13.3	97	18.0	3.1
Glomerular disease	130	24.1	112	19.8	83	15.4	−8.7
Tubulo-interstitial diseases	42	7.8	46	8.1	41	7.6	−0.2
Congenital nephrotic syndrome	27	5.0	33	5.8	35	6.5	1.5
Metabolic	29	5.4	25	4.4	31	5.7	0.4
Uncertain aetiology	12	2.2	32	5.7	29	5.4	3.1
Renovascular disease	23	4.3	19	3.4	19	3.5	−0.7
Polycystic kidney disease	16	3.0	19	3.4	19	3.5	0.6
Malignancy & associated disease	10	1.9	9	1.6	4	0.7	−1.1
Drug nephrotoxicity	14	2.6	5	0.9	0	0.0	−2.6

*Six children in 1999–2003, nine in 2004–2008 and twenty in 2009–2013 with no primary renal diagnosis recorded are excluded from this table

Table 4.14. Demographic characteristics of pre-emptive transplantation in children aged three months to 16 years in the UK between 1999–2013, analysed by 5-year time period, gender, ethnicity, age at start of RRT and primary renal diagnosis

	N	*N* (%) pre-emptively transplanted
Total cohort analysed (1999–2013)	1,212	402 (33.2)
Time period		
1999–2003	405	109 (26.9)
2004–2008	402	146 (36.3)
2009–2013	405	147 (36.3)
Gender		
Male	749	268 (35.8)
Female	463	134 (28.9)
Ethnicity		
Black	35	5 (14.3)
Other	59	19 (32.2)
South Asian	196	41 (20.9)
White	885	323 (36.5)
Age at start of RRT		
3 months–<2 years	122	6 (4.9)
2–<4 years	130	36 (27.7)
4–<8 years	206	79 (38.4)
8–<12 years	297	106 (35.7)
12–<16 years	457	175 (38.3)
Primary renal diagnosis		
Renal dysplasia ± reflux	398	168 (42.2)
Glomerular disease	217	27 (12.4)
Obstructive uropathy	215	96 (44.7)
Congenital nephrotic syndrome	81	5 (6.2)
Metabolic	73	34 (46.6)
Tubulo-interstitial diseases	71	17 (23.9)
Polycystic kidney disease	43	20 (46.5)
Renovascular disease	37	15 (40.5)
Uncertain aetiology	28	9 (32.1)
Malignancy & associated disease	14	0 (0)
Drug nephrotoxicity	10	1 (10)

and drug nephrotoxicity have fallen between 1999–2003 and 2009–2013 although in these categories absolute numbers are very small.

Pre-emptive transplantation

Of a total of 1,681 patients aged 0–16 years who started RRT between 1999 and 2013, 469 patients were excluded from this analysis (94 patients were excluded due to being aged <3 months, and a further 375 patients were excluded due to being late presenters). Of 1,212 patients identified as being aged three months to <16 years and having started RRT between 1999–2013, table 4.14 shows pre-emptive transplantation was seen to occur in 33.2% of patients and was significantly higher in males (35.8%) than females (28.9%) ($p = 0.01$). This difference is not significant however when adjusted for other factors in a logistic regression. Ethnicity was also seen to be a key factor, with children from Black (14.3%) and South Asian (20.9%) ethnicity having significantly lower rates of transplantation than their White counterparts (35.8%) ($p < 0.0001$). Analysis by age at start of RRT showed that as expected, the lowest rate of pre-emptive transplantation was in the three months to two year group (4.9%), whilst children aged four to sixteen years all had similar rates of pre-emptive transplantation. As for primary renal diagnosis, children with metabolic causes (46.6%), polycystic kidney disease (46.5%), obstructive uropathy (44.7%), renal dysplasia ± reflux (42.2%) and renovascular disease (40.5%) had the highest rates of pre-emptive transplantation, whilst those with malignancy (0.0%) had the lowest rate. Table 4.14 demonstrates the initial rise in pre-emptive transplantation rates from 26.9% in 1999–2003 to 36.3% in 2004–2008 was maintained in 2009–2013 ($p = 0.005$).

Transfer of patients to adult renal services in 2013

A total of 101 patients were reported by paediatric nephrology centres to have transferred to adult renal services in 2013. The median age of patients transferred out was 18.1 years with an inter-quartile range of 17.8 years to 18.5 years. Table 4.15 shows that of the transferred patients 60.4% were male, with ethnic minorities constituting 19.8% of patients. The vast majority (85.2%) had a functioning renal transplant at the time of transfer to an adult renal centre. Renal dysplasia ± reflux, glomerular disease and obstructive uropathy accounted for the primary renal diagnosis in over 70% of patients.

Survival of children on RRT during childhood

Of patients under 16 years of age, 1,569 were identified as starting RRT between 1999 and 2012 at paediatric centres in the UK and were included in the survival analyses. At the census date (31st December 2013) there were a total of 99 deaths reported in children on RRT under 16 years of age at paediatric centres. The median follow up time was 3.5 years (range of one day to 15 years). Table 4.16 shows the survival hazard ratios (following adjustment for age at start of RRT, gender and RRT modality) and highlights that children starting RRT under two years of age had the worst survival outcomes with a hazard ratio of 5.0 (confidence interval (CI) 2.8–8.8, $p < 0.0001$) when compared to 12–16 year olds. Outcomes in both the 2–<4 age group and the

Table 4.15. Modality, gender, ethnicity and primary renal diagnosis of patients transferred out from paediatric nephrology centres to adult renal services in 2013

	N	% distribution
Modality		
Transplant	86	85.2
HD	11	10.9
PD	4	4.0
Gender		
Male	61	60.4
Female	40	39.6
Ethnicity		
White	81	80.2
South Asian	17	16.8
Other	2	2.0
Black	1	1.0
Primary renal diagnosis		
Renal dysplasia ± reflux	30	29.7
Glomerular disease	24	23.8
Obstructive uropathy	19	18.8
Congenital nephrotic syndrome	7	6.9
Tubulo-interstitial diseases	5	5.0
Metabolic	4	4.0
Uncertain aetiology	4	4.0
Polycystic kidney disease	3	3.0
Renovascular disease	3	3.0
Drug nephrotoxicity	1	1.0
Malignancy & associated disease	1	1.0

Table 4.16. Survival hazard ratio during childhood for paediatric RRT patients aged <16 years in the UK adjusted for age at start of RRT, gender and RRT modality

	Hazard ratio	Confidence interval	*p*-value
Age			
0–<2 years	5.0	2.8–8.8	<0.0001
2–<4 years	2.9	1.4–5.7	0.003
4–<8 years	2.2	1.3–4.0	0.006
8–<12 years	1.4	0.7–2.9	0.4
12–16 years	1.0	–	–
Gender			
Female	1.2	0.7–1.9	0.5
Male	1.0	–	
RRT modality			
Dialysis	7.1	4.7–10.7	<0.0001
Transplant	1.0	–	

4–<8 age group were also significantly worse with a hazard ratios of 2.9 (CI 1.4–5.7, $p = 0.003$) and 2.2 (CI 1.3–4.0, $p = 0.006$) respectively. Being on dialysis, as expected, was seen to lower survival significantly compared to having a functioning transplant with a hazard ratio of 7.1 (CI 4.7–10.7, $p < 0.0001$). Figure 4.5 shows unadjusted Kaplan Meier (KM) survival probabilities. As the maximum age of follow up was restricted to 16 years, it was not possible to calculate 10 year survival probabilities for patients starting RRT aged >8 years, or 5 year survival probability for children starting RRT aged >12 years. This figure again highlights worse outcomes for those aged less than two years, particularly during the first year.

Mortality data in 2013

Eight deaths occurred in paediatric renal centres in 2013; of these, seven were under 16 years of age and one was aged 18 years at the time of death. In children

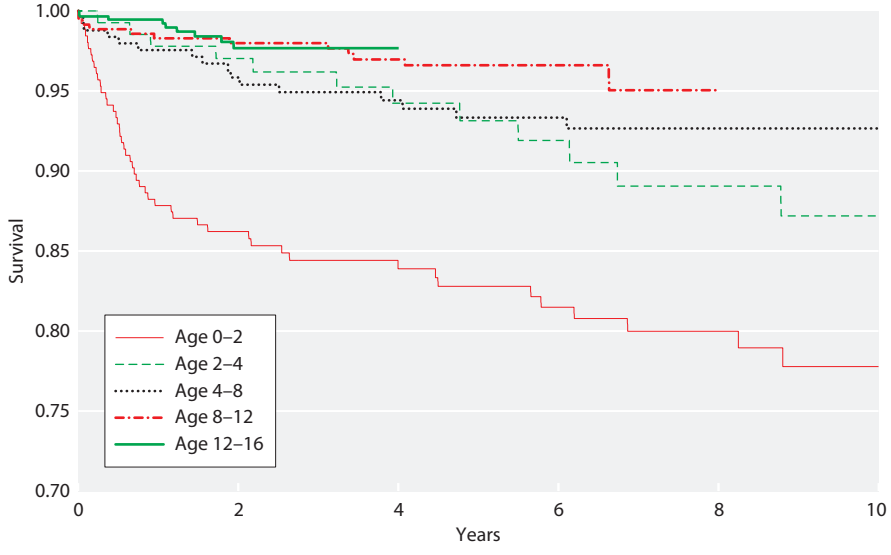

Fig. 4.5. Unadjusted KM survival in paediatric patients <16 years old starting RRT between 1999 and 2012, by age at start

aged <16 years with treated ERF, the total reported mortality in 2013 in the UK at paediatric centres was 1.0% (7/702), and 3.3% (5/152) for those on dialysis. The median age at death was 7.4 years with a range of 1.3 years to 18.0 years.

Transplant deaths

At the time of death, two children had received a kidney transplant. Infection was the cause of death in one, and the other patient died from drug related toxic epidermal necrolysis during treatment for post-transplant lymphoproliferative disorder.

Dialysis deaths

At the time of death, three children were on dialysis (two HD and one PD). Three further children died whilst receiving active palliative care (two HD and one PD). Infections were the cause of death in two patients, one of which was associated with HD and the other with PD. One patient died as a result of complications from treatment of malignancy.

Discussion

This report has focused on the current demography and the demographic trends over the past 15 years in the UK paediatric ERF population. It includes 702 children and adolescents under 16 years of age, who were receiving RRT in 2013. The sub-section on the trends in demographics includes children and adolescents under 16 years of age on RRT; 546 from 1999–2003, 575 from 2004–2008 and 560 from 2009–2013.

Data completeness

The ongoing sustained effort by clinical teams, data managers and statisticians to improve the accuracy, quality and consistency of data, analyses and conclusions continues with our aim to maintain full electronic annual returns from all centres. A revised data set (The NEW Paediatric Dataset) is in the process of being implemented and when complete will further improve registry reports.

For 2013, 100% of data were submitted electronically from the 13 paediatric nephrology centres in the UK. Data returns were complete for key data items and this together with improved checking and validation procedures within the registry contributed to continuing quality improvement. Ongoing work to merge the paediatric and adult registries will enable better identification and reporting of the 16–18 year old age group ($n = 189$ in 2013) who are not well represented in this report.

Incidence, prevalence and trends

The incidence rate of RRT in the less than 16 year age group was 9.3 pmarp in 2013; this rate has been stable since 1999. The overall prevalence rate of RRT in the less than 16 year age group was 58.2 pmarp. The prevalence of RRT increased with age and was higher in males across all age groups. Children from ethnic minorities displayed higher prevalent rates of RRT when compared with White children, with South Asian children displaying the highest rates. Overall, there was a continuing trend of increased prevalence of children on RRT with increased age, in keeping with improved survival with increasing age. Over time, the prevalent paediatric population is younger, with more children aged less than 8, and fewer aged 8–16.

Treatment modality of ERF

PD was the initial treatment modality for 45% of patients in prevalent paediatric <16 years old in 2013, 31% commenced HD and 24% received a pre-emptive transplant. Age influenced the modality of RRT with the majority of those under two (52%) receiving PD, although absolute numbers are small in this group. Overall the majority of prevalent children on RRT had a functioning transplant (78%), about half of which were deceased donors and the other half living donor transplants. Over the last 15 years, the proportion of incident paediatric patients <16 years old receiving PD as initial modality is reducing whilst proportions of those receiving HD and living kidney donation are increasing, with more younger and fewer older patients in the cohort over time.

Causes of ERF and observed trends 1999–2013

As previously, renal dysplasia ± reflux (34.2%), obstructive uropathy (18.2%), and glomerular disease (10.5%) were the commonest listed aetiologies for prevalent paediatric patients <16 years old with ERF. These accounted for 62.9% of all patients for whom a primary diagnosis had been reported. Observation of trends over the 15-year period showed an increase in the percentage of incident paediatric patients <16 years old receiving RRT with renal dysplasia ± reflux and obstructive uropathy with a fall in the percentage with glomerular disease. Further analyses are needed to understand if the proportional reduction in glomerular disease was a result of improved outcomes or a result of very young children with structural renal disease being offered

treatment. No cases of ERF secondary to 'drug nephrotoxicity' were reported this year or in the most recent 5-year period.

Comorbidities

At the onset of RRT in prevalent paediatric patients <16 years old, 32.3% of patients had one or more associated comorbidities. This overall proportion of children with reported comorbidities has fallen from 34.1% to 28.5% over the past 15 years. There continues to be significant variation in registered comorbidity rates between centres (from 89% to 36% with no registered comorbidities); it is likely that this is influenced by different reporting practices between centres, however, importantly it may reflect differing approaches to acceptance of patients with comorbidity for RRT between centres. Consequently understanding this variation remains an area for further work for the registry and individual centres.

Pre-emptive transplantation

Over the past 15 years, pre-emptive transplantation was seen to occur in 33.2% of children under 16 years of age. The improvement in rates of pre-emptive transplantation for those referred early has remained consistent over the last 10 years at 36.3%, compared to 26.9% in 1999–2003. There were significantly lower rates of pre-emptive transplantation in girls, however this difference was not present once corrected for other factors. There were significantly lower rates of pre-emptive transplantation in ethnic minorities and this would be of interest for further research. Detailed analyses of late presenters may identify other barriers to pre-emptive transplantation.

Transfer out and survival data

Although practice varied regarding transfer age between individual centres, the median age of transfer to adult services was 18.1 years in 2013. Of patients receiving RRT, 85.2% transferred with a functioning renal transplant. There were differing practices between centres regarding transition and transfer out arrangements; it is also likely that variability exists in reporting of 'transfer out' timelines to the registry for patients being transitioned to adult renal centres. Consensus regarding terminology and process will facilitate future comparative interpretation.

Survival data of children on ERF during childhood who commenced RRT between 1999 and 2012 highlights the less favourable outcome for children less than two years of age. These data also highlight the significantly better survival of children with functioning transplants when compared to those on dialysis. Further work in this area will aim to identify the reasons why patients are receiving dialysis and their barriers to transplantation. Longer term survival data up to four years was available for those aged 12 to 16 years and 10 year survival data for those aged $\leqslant$6 years of age.

Current and future work

A research project forming a collaboration between the UKRR and the University of Bristol has begun and aims to identify broad outcomes for young adults on RRT and examine the process of transition. Due to variation in the age at transfer to adult centres and the fact the adult renal centres begin reporting RRT patients once they have reached the age of 18, young adults presenting in renal centres before the age of 18 are not reported to the UKRR. The creation of datasets for young adults on RRT will be able to report much more comprehensively on the 16–18 year old age group, solve issues with patient timelines by linking those moving between paediatric and adult databases as well as establishing longer term graft outcomes for those transplanted in childhood.

Conflicts of interest: none

References

1 Pruthi R, O'Brien C, Casula A, Braddon F, Lewis M, Maxwell H, Stojanovic J, Tse Y, Inward C, Sinha MD. UK Renal Registry 16th Annual Report: Chapter 7 Demography of the UK Paediatric Renal Replacement Therapy Population in 2012. Nephron Clin Pract 2013; 125(1–4):127–38. doi: 10.1159/000360026

2 http://www.Ons.Gov.Uk/census

3 Pruthi R, O'Brien C, Casula A, Braddon F, Lewis M, Maxwell H, Tse Y, Inward C, Sinha MD. UK Renal Registry 15th Annual Report (December 2011): Chapter 4 Demography of the UK Paediatric Renal Replacement Therapy Population in 2011. Nephron Clin Pract 2013;123(suppl 1): 81–92. doi: 10.1159/000353323