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Transfusion in children: epidemiology and 10-year survival of transfusion recipients

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SUMMARY

Objective: To describe the epidemiology of blood transfusion in children: including the incidence of transfusion, the diagnoses leading to transfusion, donor exposure (DE) and post-transfusion survival.

Study design and methods: The Epidemiology and Survival of Transfusion Recipients (EASTR) Study was a multi-centre epidemiological study with prospective survival monitoring. Cross-sectional sampling of adult and paediatric transfusion recipients in 29 hospitals was used to select three separate cohorts of red cell (RBC), platelet (PLT) and fresh frozen plasma (FFP) recipients between October 2001 and September 2002. This paper presents the analysis of results for children <16 years.

Results: Children <16 years comprised 449 (5%) of the RBC, 362 (9%) of the FFP and 452 (13%) of the PLT recipients. In children 54% of RBC, 63% FFP and 45% PLT recipients were under 1 year of age and 57% RBC, 60% FFP and 52% PLT were male. Median (IQR) DEduring the study year was 3(2–8); 5(2–13) and 11(6–21) in the RBC, FFP and PLT cohorts, respectively. A total of 20% of RBC, 31% of FFP and 54% of PLT recipients had been exposed to >10 donors.

Perinatal conditions were the commonest indication for transfusion in the RBC (36%) and FFP (44%) cohorts and comprised 31% of the PLT cohort. Medical conditions (48%), predominantly malignancy (33%), were the most frequent indication in the PLT cohort. The 10 year (95% CI) survival rates were 81% (77–85%), 72% (67–76%) and 71% (66–75%)for RBC, FFP and PLT cohorts, respectively.

Conclusions: Around half of paediatric transfusion recipients are under 1 year of age. Exposure to components from multiple donors is common. At least 70% of paediatric recipients are long survivors and are at risk for late complications of transfusion.

Key words: blood transfusion, epidemiology, paediatric, survival.

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Infants and children are transfused in many clinical situations; some indications are in common with adult patients but others are unique to the physiology of infancy or disease processes found only in childhood. Understanding the frequency of transfusion in childhood and the indications for the use of transfused components is important both to paediatric clinicians wishing to optimize transfusion practice and to blood providers needing to plan the provision of blood components for children.

Little is published regarding the epidemiology of transfusion in the paediatric population. Most blood providers produce specialist components targeted to the needs of neonates and infants, but older children receive aliquots of standard blood components. It is, therefore, possible to determine how many specialist components are issued (usually to the very young) but much more difficult to understand transfusion practice in older children. A study in the Netherlands estimated that of all blood components issued 3·6% red blood cells (RBCs), 6·8% fresh frozen plasma (FFP) and 14·6% platelet (PLT) were transfused to children aged <16 years (Borkent-Raven *et al.*, 2011).

There have been two retrospective surveys of paediatric transfusion that highlighted cardiac surgery, prematurity and haematological disorders and malignancy as common disease groups associated with transfusion (Gauvin *et al.*, 2008, Slonim *et al.*, 2008). A small number of population-based surveys have included patients of all ages, including children, but none have analysed the paediatric population in detail (Wells *et al.*, 2002, Cobain *et al.*, 2007, Borkent-Raven *et al.*, 2010).

The Epidemiology and Survival of Transfusion Recipients (EASTR) study is the first national (England) study of transfusion recipients. The study identified a representative dataset of RBC, FFP and PLT recipients, to document their age, gender, blood components received and the indications for transfusion (Llewelyn *et al.*, 2009, Wells *et al.*, 2009). The study also collected prospective survival data. It is the first population-based study of blood usage that includes children from a wide range of tertiary, specialist and local hospital settings.

This paper presents an analysis of the epidemiology of the transfusion recipients that were below 16 years of age at the time of study selection. The data have been interrogated to provide information on age, sex and diagnostic groups for paediatric

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recipients and also to identify groups at greatest risk for multiple transfusion episodes (TEs) and high-donor exposure (DE). DE is the potential number of different human donors that an individual has been exposed to through blood transfusion; certain components (e.g. pooled donor platelets) are derived from more than one donor.We also present 10-year survival data for paediatric transfusion recipients.

METHODS

Study design

Detailed descriptions of the methodology and validation of the EASTR data collection are presented elsewhere (Llewelyn *et al.*, 2009, Wells *et al.*, 2009). Briefly, the work entailed a multi-centre epidemiological study with cross sectional sampling of transfusion recipients (from all transfusion records) over 1 year, with prospective survival monitoring. Three cohorts of patients (RBC, FFP and PLT) were sampled over a 12-month period (1 October 2001–30 September 2002) according to the blood component transfused at their index transfusion. These patients were from a representative selection of hospitals in England that received their blood components from the national blood provider, NHS Blood and Transplant. Transfusion recipients were selected for study based on a monthly quota of all recipients in each hospital.

Based on pilot study data obtained in early 2001, the cohort selection structure was designed to ensure that sufficient patients were chosen to allow characterisation of the most frequent indications for RBC, FFP and PLT transfusion. It was acknowledged that in each cohort, individual patients would, have commonly received more than one component type during a TE and study year. The sample size allowed for adequate representation from hospitals of all sizes supplied by NHSBT, with seasonal variation taken into account by monthly sampling across the year.

A TE was defined as a calendar day during which one or more blood components were issued for a patient. The TE used to select a recipient for inclusion in the study was defined as the index transfusion and the hospital admission at the time of selection denoted the index admission. Data on all components transfused during the index admission and throughout the study year were collected for patients in each cohort. Corresponding data were obtained from the hospital Patient Administration System for each patient including International Statistical Classification of Diseases (ICD-10) diagnostic codes and Office of Population Censuses and Surveys Calssification of Surgical Operations and Procedures (OPCS-4) codes for surgical and other procedures.

Allocation of the indication for transfusion

Paediatric cases were analysed independently from the adult cases. The indication for transfusion was ascribed after examining all the ICD-10 and OPCS-4 codes in the index admission, using a structured approach. These fell into three main groups, namely perinatal conditions, surgery (including trauma) or medical conditions. Where the predominant reason for admission related to prematurity, low-birth weight or problems relating to delivery, the admission was allocated to one of the perinatal subgroups. Infants in this group were those who had ICD-10 codes P00-96 for conditions originating in the perinatal period. The subgroup for extreme prematurity/extreme low birthweight (ELBW) was allocated to those with ICD-10 codes for BW <1000 g or gestation <28 completed weeks. The subgroup for prematurity/low birthweight (LBW) was allocated to those with ICD-10 codes for birthweight 1000–2499 g or gestation 28–36 completed weeks. Infants with a diagnosis primarily due to a perinatal problem but outside these subgroups were allocated to the 'other perinatal' subgroup. Children presenting within the neonatal period (<28 days) but without problems specifically relating to birth or the perinatal period were allocated to either a surgical or medical subgroup. Those children for whom a surgical procedure (as defined through a relevant OPCS-4 code) was the predominant reason for admission were allocated to one of the surgical subgroups and the remaining children were assigned to one of the medical subgroups.

Analysis

DE was calculated from the number of units transfused as follows. Transfusion from a standard adult sized pack of RBCs or FFP counted as a single DE. Each unit of PLTs was counted as exposure to 2·8 donors. This reflects the fact that at the time of the study 60% of PLT doses were manufactured from pools of four donations, whereas the remaining 40% were from apheresis collection from a single donor. For neonates and infants components were variably provided as splits of four or six from a single donation. For the purposes of this study, transfusion of each split was considered as a separate unit and DE.

Survival data was collected prospectively through the NHS Demographic Batch Service. Survival curves were obtained using the Kaplan–Meier method and curves were compared using a log-rank test. Survival was calculated from the date of the index transfusion.

Data were analysed using SAS (for Windows) version 9·3 (SAS Institute Inc., Cary, NC, USA). The study was approved by the Eastern Multi-Centre Research Ethics Committee with local hospital R&D approval and additional approval by the Patient Information Advisory Group.

RESULTS

At the 29 hospitals participating in the study a total of 68,600 recipients of all ages were transfused during the study year. A total of 9142 RBC, 4232 FFP and 3584 PLT recipients were sampled (Wells *et al.*, 2009). Of these 449 (5%) RBC, 362 (9%) FFP and 452 (13%) PLT were below 16 years of age and were included in this analysis. These groups were made up from a total of 1020 individual recipients. A total of 82·0% of paediatric recipients were transfused in large specialist hospitals (with 16·8% in medium and 1·3% in small hospitals).

Entry into the three cohorts was based on an index transfusion (in the index TE) of one component type, but many of the

children received more than one component during the study year. Overall the RBC group received a total of 3000 transfused units (2098 RBC, 322 FFP and 580 PLT), the FFP group received 3790 (1946 RBC, 1023 FFP and 821 PLT) and the PLT group received 5582 (2706 RBC, 694 FFP and 2182 PLT).

In the RBC group, the majority 282/449 (63%) of recipients received RBCs alone during the study year. In the FFP and PLT cohorts receipt of multiple components was more common with only 78/362 (22%) and 90/452 (20%) of recipients respectively receiving a single component type. Of 362 FFP cohort 40 (11%) received cryoprecipitate.

Demographics of paediatric transfusion recipients

Figure 1A–C show the age and gender distribution for each cohort. In the RBC cohort 244/449 (54%) were <1 year as were 229/362 (63%) of the FFP and 205/452 (45%) of the PLT cohorts. Neonates (that is individuals aged <28 days at index transfusion) comprised 165/449 (37%) of the RBC, 184/362 (51%) of the FFP and 148/452 (33%) of the PLT cohorts. The median age at transfusion was 155 days (IQR 6 days – 7 years) for the RBC, 25 days (IQR 1 day – 4 years) for the FFP and 2 years (IQR 11 days - 9 years) for the PLT cohorts.

There was a gender differential among recipients with 256/449 (57%) of the RBC, 213/362 (60%) of the FFP and 234/452 (52%) of the PLT cohorts being male. The general population under 16 years in 2001 comprised 51% males and 49% females (Office for National Statistics Census-2001, 2005).

Indications for transfusion

The diagnostic groupings of paediatric transfusion recipients are detailed in Table 1.

Non-surgical (medical and perinatal) indications exceed surgical in each of the three cohorts. This is especially apparent in the PLT cohort, where only 11% of recipients were transfused for surgery. Cardiac surgery was the largest individual surgical sub-group in each of the three cohorts. Trauma was responsible for 21/101 (20·7%) of all surgical patients in the RBC group, but contributed relatively little to the FFP and PLT surgical cohorts.

Transfusion for perinatal causes (especially for ELBW/LBW babies) is the largest diagnostic group within the RBC and FFP cohorts. In the platelet cohort the commonest group is medical (especially malignancy) but perinatal causes represent 31% of the recipients. In the perinatal group FFP was given earliest in the course [median 1d, interquartile range (IQR) 1–4] with RBC also given early (median 3d, IQR 1–23). Platelets were given somewhat later (median 7d, IQR 3–20).

Transfusion episodes (TE) and Donor Exposure (DE)

These data are summarised in Table 1. Annual figures for TEs, and DE may be underestimated for infants born within the study year, for whom a complete year of data was unavailable. Recipients in the PLT cohort had the highest median number

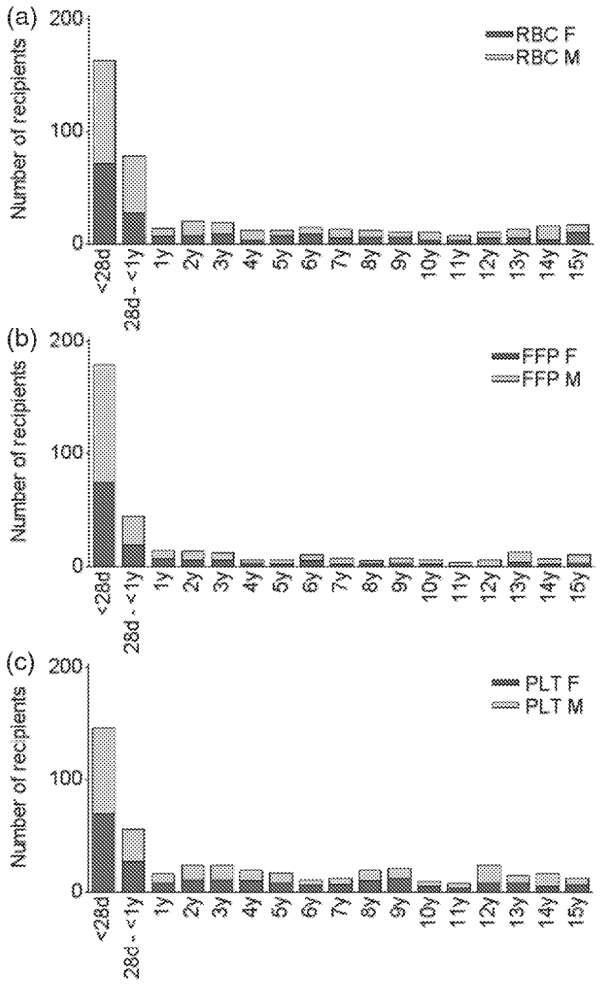

Fig. 1. Age (at index transfusion) and sex distribution of children in the RBC (A), FFP (B) and PLT (C) cohorts.

of TE during the study year, this trend is especially apparent in the medical group. For the RBC cohort, higher median TE were found in the ELBW and medical malignancy subgroups.

The median number of component-specific units (i.e. individual RBC units or single split from a split-pack in the RBC cohort) given were similar for each group (RBC 2, IQR 1–5·5, FFP Median 2, IQR 1–3, PLT Median 2, IQR 1–5). However overall DE due to all components transfused was highest in the PLT cohort (RBC Median 3, IQR 2–8, FFP Median 5, IQR 2–12·6, PLT Median 11, IQR 5·6–20·7).

In all cohorts, patients diagnosed with medical malignancies had the highest median annual DE from all components transfused followed by extremely premature/low birth weight neonates. Annual DE >10 occurred relatively frequently, but was greatest in the PLT cohort. Patients with medical malignancy were at greatest risk of annual DE > 10 in each of the cohorts. In the FFP and PLT cohorts recipients with trauma or undergoing 'other' surgical procedures were also at greater risk of annual DE > 10.

Table 1. Clinical indications for transfusion, transfusion episodes (TE) and donor exposure (DE) for each cohort

			Age		Transfusion episodes		Number receiving 1 U		Number receiving >4 U		Annual donor exposure from all components		Number with annual donor exposure > 10	
	N	(%)	Median	(IQR)	Median	(IQR)	*N*	(%)	*N*	(%)	Median	(IQR)	*N*	(%)
(a) RBC recipients by diagnostic group and sub-group														
Perinatal	163	(36)	3 days	(1–23)	2·0	(1·0–3·0)	49	(30)	46	(28)	3·0	(1·0–7·0)	22	(13)
Extremely premature/ELBW	48	(11)	2	(1–12)	3·0	(2·0–6·0)	5	(10)	24	(50)	5·5	(2·5–11·5)	13	(27)
Premature/LBW	77	(17)	7	(2–26)	1·0	(1·0–2·0)	34	(44)	15	(19)	2·0	(1·0–5·0)	8	(10)
Other perinatal	38	(8)	4	(1–23)	1·5	(1·0–3·0)	10	(26)	7	(18)	2·5	(2·0–5·0)	1	(3)
Medical	**142**	**(32)**	**5 years**	**(2–10)**	**2·0**	**(1·0–5·0)**	**35**	**(25)**	**53**	**(37)**	**4·8**	**(2·0–20·8)**	**56**	**(39)**
Malignancy	54	(12)	6·5	(4–10)	3·0	(2·0–6·0)	7	(13)	29	(54)	15·5	(4·8–29·6)	34	(63)
Haematology	36	(8)	8	(5–14)	2·0	(1·0–9·0)	7	(19)	14	(39)	6·5	(2·0–23·4)	14	(39)
Other medical	52	(12)	2	(0–7)	1·0	(1·0–2·0)	21	(40)	10	(19)	2·0	(1·0–4·4)	8	(15)
Surgery	**101**	**(22)**	**5 years**	**(0–11)**	**1·0**	**(1·0–1·0)**	**33**	**(33)**	**15**	**(15)**	**3·0**	**(1·0–6·8)**	**11**	**(11)**
Cardiac surgery	27	(6)	0	(0–6)	1·0	(1·0–1·0)	8	(30)	2	(7)	4·0	(2·0–7·8)	1	(4)
Other surgical	37	(8)	3	(0–8)	1·0	(1·0–2·0)	15	(41)	8	(22)	2·0	(1·0–7·0)	7	(19)
Neurosurgery	8	(2)	2	(0–8)	1·0	(1·0–2·0)	2	(25)	1	(13)	2·0	(1·5–5·3)	0	(0)
Orthopaedic surgery	8	(2)	12	(10–14)	1·0	(1·0–1·0)	3	(38)	0	(0)	2·0	(1·0–2·0)	1	(13)
Trauma	21	(5)	9	(3–14)	1·0	(1·0–2·0)	5	(24)	4	(19)	3·0	(2·0–5·0)	2	(10)
Unknown	43	(10)	0	(0–6)	1·0	(1·0–2·0)	10	(23)	8	(19)	3·0	(2·0–4·0)	3	(7)
Total	**449**	**(100)**	**0 years**	**(0–7)**	**1·0**	**(1·0–3·0)**	**127**	**(28)**	**122**	**(27)**	**3·0**	**(2·0–8·0)**	**92**	**(20)**
(b) FFP recipients by diagnostic group and sub-group														
Perinatal	159	(44)	1 day	(1–4)	1·0	(1·0–2·0)	83	(52)	18	(11)	6·0	(2·0–12·0)	48	(30)
Extremely premature/ELBW	52	(14)	1·5	(1–5)	1·0	(1·0–2·5)	26	(50)	7	(13)	10·0	(5·0–17·5)	24	(46)
Premature/LBW	63	(17)	1	(0–4)	1·0	(1·0–2·0)	31	(49)	5	(8)	5·0	(2·0–11·0)	17	(27)
Other perinatal	44	(12)	1	(1–3)	1·0	(1·0–2·0)	26	(59)	6	(14)	4·0	(1·0–8·0)	7	(16)
Medical	**68**	**(19)**	**3·5 years**	**(1–11)**	**1·0**	**(1·0–2·0)**	**24**	**(35)**	**9**	**(13)**	**4·9**	**(2·0–23·7)**	**31**	**(46)**
Malignancy	18	(5)	7	(3–10)	1·0	(1·0–2·0)	4	(22)	0	(0)	22·8	(10·8–64·6)	14	(78)
Haematology	6	(2)	8	(0–12)	1·0	(1·0–2·0)	3	(50)	0	(0)	4·0	(2·0–23·4)	2	(33)
Other medical	44	(12)	2	(0–9)	1·0	(1·0–2·0)	17	(39)	9	(20)	4·0	(2·0–14·7)	15	(34)
Surgery	**103**	**(28)**	**3 years**	**(0–9)**	**1·0**	**(1·0–1·0)**	**43**	**(42)**	**20**	**(19)**	**5·8**	**(3·0–10·8)**	**27**	**(26)**
Cardiac surgery	55	(15)	1	(0–4)	1·0	(1·0–1·0)	33	(60)	2	(4)	3·8	(3·0–7·0)	5	(9)
Other surgical	26	(7)	6	(0–9)	1·5	(1·0–3·0)	4	(15)	14	(54)	10·3	(3·0–37·0)	13	(50)
Neurosurgery	8	(2)	4·5	(2–11)	1·0	(1·0–1·0)	3	(38)	0	(0)	9·9	(6·8–12·1)	4	(50)
Orthopaedic surgery	7	(2)	13	(12–13)	1·0	(1·0–1·0)	1	(14)	1	(14)	8·0	(5·8–13·6)	2	(29)
Trauma	7	(2)	14	(7–15)	1·0	(1·0–2·0)	2	(29)	3	(43)	10·0	(5·0–30·4)	3	(43)
Unknown	32	(9)	0	(0–4)	1·0	(1·0–1·0)	15	(47)	2	(6)	3·0	(1·0–8·8)	7	(22)
Total	**362**	**(100)**	**0 years**	**(0–4)**	**1·0**	**(1·0–2·0)**	**165**	**(46)**	**49**	**(14)**	**5·0**	**(2·0–12·6)**	**113**	**(31)**
(c) PLT recipients by diagnostic group and sub-group														
Perinatal	**142**	**(31)**	**7 days**	**(3–20)**	**2·0**	**(1·0–3·0)**	**64**	**(45)**	**27**	**(19)**	**8·8**	**(4·0–17·0)**	**62**	**(44)**
Extremely premature/ELBW	56	(12)	9	(4–20)	2·0	(1·0–4·0)	20	(36)	15	(27)	13·9	(7·5–24·4)	36	(64)
Premature/LBW	54	(12)	7·5	(3–21)	1·0	(1·0–3·0)	30	(56)	8	(15)	5·3	(2·8–11·0)	16	(30)
Other perinatal	32	(7)	4	(2–13)	1·0	(1·0–2·0)	14	(44)	4	(13)	6·0	(3·4–13·0)	10	(31)
Medical	**216**	**(48)**	**6 years**	**(3–10)**	**2·5**	**(1·0–5·0)**	**56**	**(26)**	**80**	**(37)**	**13·6**	**(6·8–24·6)**	**133**	**(62)**
Malignancy	149	(33)	7	(3–10)	3·0	(1·0–5·0)	33	(22)	57	(38)	14·2	(7·8–23·8)	99	(66)
Haematology	31	(7)	5	(2–11)	3·0	(1·0–6·0)	8	(26)	12	(39)	9·4	(2·8–24·8)	14	(45)
Other medical	36	(8)	2	(0–9)	1·0	(1·0–3·0)	15	(42)	11	(31)	11·6	(4·8–25·8)	20	(56)
Surgery	**51**	**(11)**	**3 years**	**(0–13)**	**1·0**	**(1·0–1·0)**	**31**	**(61)**	**7**	**(14)**	**9·8**	**(6·8–16·0)**	**25**	**(49)**
Cardiac surgery	20	(4)	0	(0–3)	1·0	(1·0–1·0)	19	(95)	0	(0)	7·9	(5·3–9·8)	4	(20)
Other surgical	17	(4)	2	(0–8)	2·0	(1·0–6·0)	5	(29)	6	(35)	14·8	(10·6–47·6)	14	(82)
Neurosurgery	4	(1)	13·5	(8–15)	1·0	(1·0–1·0)	1	(25)	0	(0)	9·7	(7·6–11·7)	2	(50)
Orthopaedic	5	(1)	13	(13–14)	1·0	(1·0–1·0)	3	(60)	0	(0)	8·8	(7·8–13·6)	2	(40)
Trauma	5	(1)	8	(8–15)	1·0	(1·0–1·0)	3	(60)	1	(20)	12·8	(6·8–30·4)	3	(60)
Unknown	43	(10)	0	(0–7)	1·0	(1·0–3·0)	18	(42)	6	(14)	12·4	(4·8–16·0)	23	(53)
Total	**452**	**(100)**	**2 years**	**(0–8)**	**2·0**	**(1·0–4·0)**	**169**	**(37)**	**120**	**(27)**	**11·0**	**(5·6–20·7)**	**243**	**(54)**

Use of neonatal and standard components

In each cohort the majority of neonatal recipients received each component in the form of neonatal specification 'split packs' [134/165 (81%) RBC, 126/184 (68%) FFP and 114/148 (77%)] of PLT. The remaining neonates received at least a portion of their transfusions as standard components.

Survival of transfused patients

Figure 2 presents survival curves for paediatric patients transfused during this study for each recipient group, by age group and the associated data are contained within Table 2. In each of the recipient groups, there is a greater proportion of early deaths among those who received their index transfusion as neonates

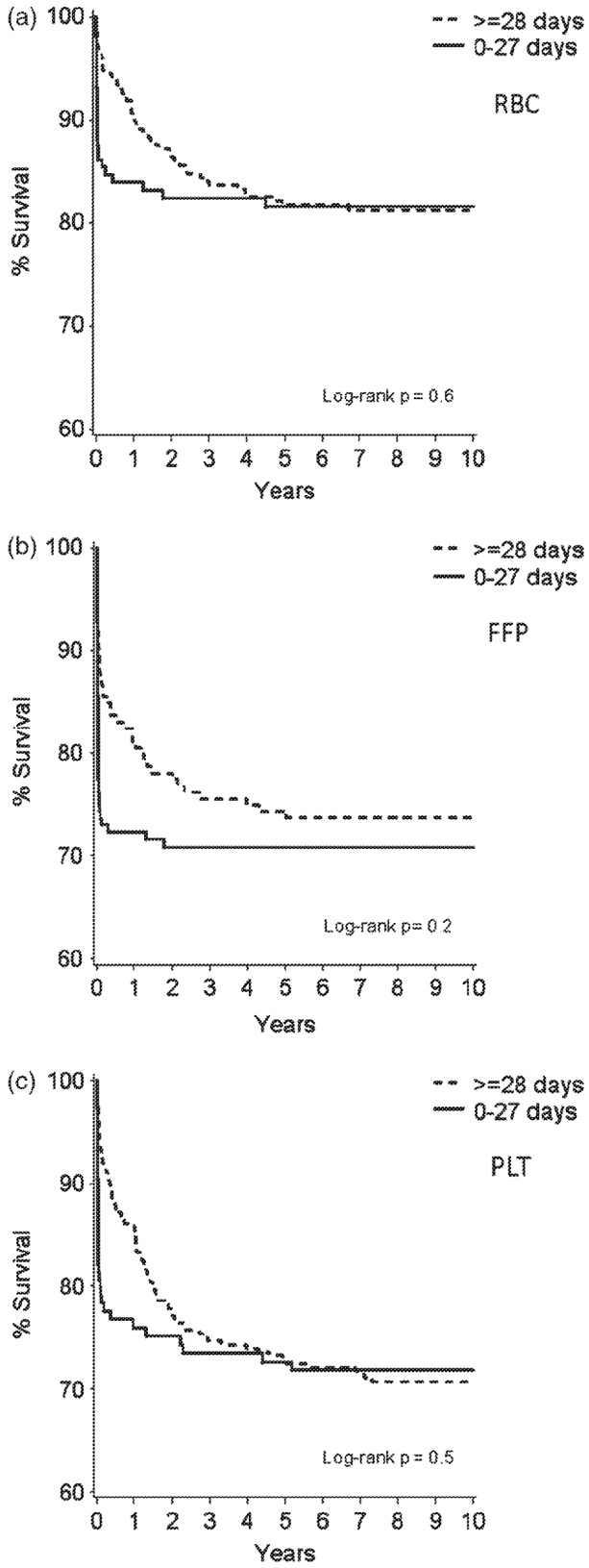

Fig. 2. Survival curves (from the date of the index transfusion) of children in the RBC (A), FFP (B) and PLT(C) cohorts.

(within the first 28 days of life). The difference in the survival at 10 years post enrolment for neonates versus older children was not statistically significant for any of the recipient groups.

DISCUSSION

Analysis of the EASTR study (including all adult and paediatric recipients) has shown that 5% of RBC, 9% of FFP and 13% of PLT recipients fall within the paediatric age group (i.e. under 16 years of age) (Llewelyn *et al.*, 2009; Wells *et al.*, 2009). A total of 7% of all transfusion recipients identified in the study hospitals during the study year were under 16 years of age (4% were <1 year of age). It was estimated that nationally 16,350 children received RBCs, 4896 received FFP and 5049 received platelets during the study year (Wells *et al.*, 2009). The 2001 National census for England and Wales (Office for National Statistics Census-2001, 2005) recorded 10,488,736 children under 16 years in England and Wales and this group comprised 20·1% of the population. There were 589,100 (1·1% of the population) under 1 year of age. This suggests that overall children are under-represented among transfusion recipients as compared to adults, although children under 1 year are over-represented as compared to older children and adults.

The acute hospitals selected for the study were chosen to be representative for hospital admissions across all age groups and were responsible for 17·7% of inpatient episodes in children under 16 years in England during the study period. They contributed 18·4% of national admissions for children up to 28 days of age, suggesting a representative age structure within the paediatric group. The representation of specialist paediatric services was also comparable (e.g. 21% of premature and LBW babies and 18·3% of those with malignancies). There was some under-representation of cardiac surgical admissions with only 11·1% of the national admissions in this group of hospitals and therefore transfusions attributable to paediatric cardiac surgery may be underestimated.

The RBC and FFP cohorts contain a higher proportion of males than females. This male preponderance is maintained across all the major diagnostic groups. Membership of the PLT cohort shows no gender differential. The reasons for the excess of males in the RBC and FFP cohorts is unclear but the predominance of male transfusion recipients in childhood equates well to the excess of males admitted to hospital and intensive care in that group (Hospital Episode Statistics Online). Female RBC recipients exceed males from 15 years of age onwards (Wells *et al.*, 2009); although none of the paediatric cases had diagnoses directly attributable to gynaecological or obstetric problems, the post-pubertal girls would be expected to have a lower total red cell mass (due to the onset of menstruation).

Relatively little has been published regarding the indications for transfusion in children. Slonim *et al.* (2008) determined that 4·8% of inpatients in specialist paediatric hospitals in the United States received blood component transfusions. Commonly highlighted diagnoses were agranulocytosis and chemotherapy recipients, sickle cell disease, leukaemia and respiratory distress

Table 2. Percentage survival of children transfused in each cohort

Group	Age at entry	1 month survival	Log-rank *p*	1 year survival	Log-rank *p*	5 year survival	Log-rank p	10 year survival	Log-rank p
RBC ($n = 449$)	All	92·7(89·8–94·8)		87·9(84·4–90·7)		81·4(77·3–84·9)		81·1(77·0–84·6)	
	<28 days	86·2(79·7–90·7)	<0·0001	83·9(77·1–88·9)	0·02	81·6(74·4–86·9)	0·5	81·6(74·4–76·0)	0·6
	> = 28 days to <16 years	96·4(93·4–98·0)		90·3(86·1–93·3)		81·7(76·5–85·9)		81·3(76·0–85·6)	
FFP ($n = 362$)	All	80·7(76·2–84·5)		76·5(71·6–80·7)		72·2(67·0–76·7)		71·8(66·6–76·4)	
	<28 days	73·7(66·5–79·6)	0·0007	72·3(65·0–78·4)	0·02	70·8(63·3–77·1)	0·2	70·8(63·3–77·1)	0·2
	> = 28 days to <16 years	87·9(82·0–91·9)		81·2(74·4–86·3)		74·4(67·0–80·3)		73·7(66·3–79·8)	
PLT ($n = 452$)	All	89·4(86·2–91·9)		82·5(78·5–85·7)		72·5(68·0–76·5)		70·8(66·2–74·9)	
	<28 days	79·9(72.4–85·6)	<0·0001	75·9(68·0–82·2)	0·003	72·6(64·3–79·3)	0·4	71·8(63·4–78·6)	0·5
	> = 28 days to <16 years	94·0(90·7–96·2)		85·7(81·2–89·3)		72·9(67·3–77·6)		70·7(65·1–75·6)	

syndrome. Gauvin *et al.* (2008) retrospectively reviewed 1100 cases transfused between 1990 and 1992 at a single large specialist children's hospital in Canada. The commonest indications for transfusion were cardiac disease 22·1%, prematurity 21·6% and malignancy 10·9%. These two studies report data only from specialist children's centres and therefore include only the more complex paediatric cases.

Our study has demonstrated that patients with perinatal disorders and particularly those born preterm are the largest transfusion recipient group in the paediatric population served by NHSBT. Within this group the most premature are at greatest risk of multiple TEs and high DE. The majority receive their first transfusion within the first 7 days of life. In the UK, and many other countries, components for children under 1 year of age are commonly provided as split packs (i.e. multiple smaller packs of a component derived from a single donation). How these packs are used is dependent on the individual hospital. In the case of RBCs, where multiple top-up transfusions are likely to be required then a hospital may reserve all the packs from one donation for use in that child (with the aim of minimizing DE), although practice varies. Split packs of PLTs and FFP are less commonly managed in this way. Our findings support the continued provision of components for transfusion in 'split packs' for neonates and infants and also the use of single donor (rather than pooled) platelets for all children to reduce DE. Patients with malignancy are the next most transfused sub-group. They are at high risk for multiple TEs and the majority of children with malignancies had DE > 10 during the study year. Cardiac surgical cases contributed the largest number of recipients due to surgery in each cohort.

Many transfused children had multiple TEs and the majority of those transfused received more than one unit/split pack during the study year. A considerable proportion of recipients were also estimated to have total DE during the study year of >10. Higher DE may be linked to higher mortality (Gauvin *et al.*, 2008) but also places the recipient at greater risk for unwanted effects of transfusion.

PLT recipients had higher DE often across multiple TEs. Higher DE may be partly due to the use of platelet pools (made from four donations) as well as single donor apheresis platelets. Many platelet recipients have long-term conditions causing bone marrow failure. The high DE in this group supports the more recent NHSBT policy that aims to provide single donor platelet units to all children.

Little information on survival following transfusion is available, especially for children. A regional study in the north east of England reviewed the survival of a group of 2899 patients transfused in June 1994 of whom 180 were below 20 years of age. In this sample 5-year survival of children under 1 year of age was 78%, between 1 and 9 years of age was 85% and between 10 and 19 years of age was 78% (Wallis *et al.*, 2004). In a group of 1100 children with a median age of 16 months (range 0–17 years) transfused in a single large children's hospital in Canada between 1990 and 1992 (Gauvin *et al.*, 2008), survival was 83·6% at 5 years and 82·3% at 10 years. Children transfused as neonates and heavily transfused patients exhibited higher mortality. Because this study was undertaken at a single tertiary centre, with many high-risk cases it is difficult to extrapolate this to the wider paediatric population. A more recent retrospective study in the Netherlands estimated that 10-year survival for children ranged from 77 to 83% for RBC transfusion, with lower rates for FFP (69–75%) and PLT (45–68%) transfusion (Borkent-Raven *et al.*, 2010).

In our study the greatest survival at 10 years also occurs in the RBC cohort with 81·6% survival for those enrolled as neonates versus 81·3% for those >28 days. The 10-year survival for the FFP and PLT cohorts were: FFP neonates 70·8% versus older children 73·7% and PLT neonates 71·8% versus older children 70·7%. Our study also demonstrates significantly increased early mortality in those transfused as neonates, as compared with those transfused as older children. These differences are no longer apparent at 5–10 years. Paediatric PLT recipients appear to have slightly higher survival rates in the UK as compared to the Netherlands. The variation in survival between these studies

may reflect differences in transfusion or clinical practice or in case identification.

This paper presents the first population based analysis of paediatric transfusion epidemiology. It included patients in the complete range of hospital care settings, from small district hospitals to large tertiary centres. Although transfusion in childhood is less common than for adults, neonates and infants are more likely to be transfused. Many transfused children are at risk of high DE that may contribute to unwanted effects in later life. This study did not attempt to assess the appropriateness of the transfusions given, but research in this area is clearly important in those groups at highest risk of transfusion.

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