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Transfusion in adults: 10-year survival of red cell, plasma and platelet recipients following transfusion

S. L. Morley,[1] C. L. Hudson,[1] C. A. Llewelyn,[1] A. W. Wells,[2] A. L. Johnson,[3] L. M. Williamson[1] & for the EASTR study group

[1]*Cambridge Blood Centre, NHS Blood and Transplant, Cambridge, UK,* [2]*Scottish National Blood Transfusion Service, Edinburgh, UK, and* [3]*MRC Clinical Trials Unit, University College London, London, UK*

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SUMMARY

Objective: To determine the long-term survival of adult recipients (>16 years) transfused with red blood cells (RBC), platelets (PLT) and fresh frozen plasma (FFP) in England and Wales.

Study design and methods: The EASTR study (Epidemiology and Survival of Transfusion Recipients) was a national multi-centre epidemiological study with cross-sectional sampling from 29 representative hospitals in England supplied by NHS Blood and Transplant (NHSBT). Three separate groups of RBC ($n = 9142$), FFP ($n = 4232$) and PLT (3584) recipients were sampled over 1 year (1 October 2001–30 September 2002), with prospective survival monitoring for 10 years. This study presents the data for adult recipients (>16 years of age).

Results: The median age interquartile range (IQR) of adult transfusion recipients was RBC 70 (54–79), FFP 66 (51–76), PLT 62 (48–72). The 10-year survival for adult RBC, FFP and PLT recipients was highest for RBC recipients at 36% confidence interval (CI 35–37%, $n = 8675$), compared with 30% for both FFP (CI 29–32%, $n = 3849$) and PLT (CI 28–30%, $n = 3110$) recipients. In all groups, post-transfusion survival decreased with age, and a risk-adjusted analysis showed that reason for transfusion, transfusion type (surgical or medical) and cancer diagnosis (presence or absence) were all significantly associated with survival. Older patients with cancer receiving a medical rather than surgical transfusion had the highest hazard of death.

Conclusion: This study shows that survival following transfusion in England is broadly similar to that reported in other wealthy nations. More than 70% of recipients die within 10 years of transfusion, but long-term survival is common in younger patients (>80% 10-year survival in RBC recipients aged 16–39 years).

Key words: blood transfusion, epidemiology, survival.

Correspondence: Dr Sarah L. Morley, NHS Blood and Transplant, Long Road, Cambridge CB2 0PT, UK.
Tel.: + GRO-C fax: + GRO-C e-mail: GRO-C

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Understanding the risks and benefits of transfusion is key to inform future clinical guidance and determine cost effectiveness of safety initiatives. In acute haemorrhage, transfusion can be life saving, but in other settings, the benefits are less well defined. Many of the specific side effects of transfusion are well documented; the majority take effect in the short term (acute transfusion reactions), but some have medium- to long-term implications (predominantly transfusion-transmitted infection or TTI). Interventions to reduce TTI have added significantly to the cost of transfused blood components (Jackson *et al.*, 2003; Dorsey *et al.*, 2014). The cost-effectiveness of these interventions is important to estimate, but one key factor in establishing this for infections with long-delayed clinical consequences is to understand survival post-transfusion. Understanding the influences of age, component transfused and indication for transfusion on survival may allow specific interventions to be applied only to the recipient groups where they will be most clinically and cost effective.

Transfusion of human blood components is a complex intervention, when considered as an infusion of numerous antigenic and bioactive substances. It is also usually undertaken as part of a series of complex interventions during a course of treatment. This can make it difficult to understand the influence of transfusion in positive and negative outcomes. There is evidence that transfusion can contribute to poor post-operative and intensive care outcomes (Hopewell *et al.*, 2013; Rohde *et al.*, 2014). Determining long-term outcomes (including long-term survival) in transfusion is essential for the complete understanding of the overall risks and benefits.

There have been a number of studies of survival after transfusion undertaken in recent decades (Tynell *et al.*, 2001; Vamvakas & Goldstein, 2002; Wallis *et al.*, 2004; Gauvin *et al.*, 2008; Kamper-Jorgensen *et al.*, 2008; Borkent-Raven *et al.*, 2011; Dorsey *et al.*, 2014). Most are based upon retrospective review of clinical databases. The EASTR study is the first prospective national study of transfusion recipients. The study identified a representative dataset of red blood cells (RBC), fresh frozen plasma (FFP) and platelets (PLT) recipients, and has previously reported their age profile, gender, blood components received and the indications for transfusion (Llewelyn *et al.*, 2009, Wells

et al., 2009). The study also collected prospective survival data, and this paper presents an analysis of the survival of patients transfused in each of the component groups to 10 years and considers the influence of age at transfusion and diagnosis on survival.

METHODS

Study design

The EASTR study was a multi-centre epidemiological study with a cross-sectional sample of transfusion recipients (adults and children) over 1 year and prospective survival monitoring (Llewelyn *et al.*, 2009, Wells *et al.*, 2009). This paper describes adult (recipients aged 16 years or over) 10-year survival after transfusion. 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 (from small district to large teaching hospitals) in England who 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 and survival outcomes 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 transfusion episode (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 ICD-10 (International Statistical Classification of Diseases) diagnostic codes and OPCS-4 (Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures) codes for surgical and other procedures.

The study was approved by the Eastern Multi-Centre Research Ethics Committee, with local hospital R&D approval and additional Section 60 approval by the National Information Governance Board (formerly the Patient Information Advisory Group).

Allocation of the indication for transfusion

The methods used to match blood bank transfusion data with hospital PAS records and to allocate the most representative transfusion indication based on scrutiny of all diagnostic and procedural codes present during the index admission have been described in detail elsewhere (Llewelyn *et al.*, 2009; Wells *et al.*, 2009). Briefly, adult patients were allocated to one of several EASTR case-mix groups (eCMGs), broadly corresponding to clinical specialties associated with major blood use. These were cardiac, digestive, hepatobiliary (including pancreas), haematology, musculoskeletal, obstetrics and gynaecology (O&G), renal tract, respiratory, vascular, trauma and other groups. With the exception of haematology (where all patients were transfused for medical conditions) and the cardiac and vascular eCMGs (where almost all recipients were transfused in association with major surgical procedures), eCMGs contained varying proportions of medical and surgical patients. Patients were therefore flagged according to presence or absence of major surgical procedural and cancer diagnostic codes within the index admission to allow for stratification for these variables in addition to gender and eCMG group during the analysis. In this survival analysis, the digestive and hepatobiliary eCMGs have been combined into one eCMG, and results for the O&G eCMG only presented for the RBC group due to insufficient numbers in the PLT and FFP groups.

Obtaining survival data

Survival was monitored prospectively through the NHS Demographic Batch Service (formerly the National Strategic Tracing Service).

Statistical analysis

Survival was calculated using time from index transfusion to last known follow-up or death, whichever was earlier.

Survival functions were calculated for each component group for overall survival and also stratified according to age group, eCMG, gender, indication for transfusion during the index admission (medical or surgical) and cancer (presence or absence) during the index admission. Survival curves were obtained using the Kaplan–Meier method and were compared using a log-rank test.

Risk-adjusted analyses were performed using Cox proportional hazards regression modelling. Factors considered for risk adjustment were age group, eCMG, gender, indication for transfusion and cancer. The lower two age groups (16–24, 25–39) were combined as hazard ratios for these were similar. The eCMGs were also compressed; digestive, hepatobiliary and pancreas, musculoskeletal, trauma and renal tract eCMGs were all included in the 'other' category. The modelling of interactions

between the factors was considered, but there were insufficient numbers of deaths to be able to estimate those that were significant. The prediction accuracies of the models with and without interaction terms were compared using the Kent O'Quigley Prediction Accuracy Measure (Kent *et al.*, 1988), and little difference was found.

Data were analysed using SAS (for Windows) version 9 (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 Section 60 approval by the National Information Governance Board (formerly the Patient Information Advisory Group).

RESULTS

At the 29 hospitals participating in the study a total of 68 600 transfusion recipients of all ages were identified during the study year, and 9142 RBC, 4232 FFP and 3584 PLT recipients were sampled during the study (Wells *et al.*, 2009). Of the RBC recipients, 8675 (95%) , 3849 (91%) of the FFP recipients and 3110 (87%) of the PLT recipients were aged 16 years or over and were included in this analysis. Duplicate patients and patients with unknown age were removed from the cohort. The three groups made up a total of 13 258 individual recipients.

Entry into the three recipient groups was based on an index transfusion of one specific component, but many of the patients received more than one component during the study year. The majority (86%) of RBC recipients received RBCs alone, whereas FFP and PLT recipients were more likely to have received multiple components; 57% of FFP recipients received only FFP and 53% of PLT recipients only received PLTs. These results reflect the sampling methodology in which a high proportion of patients were sampled independently for inclusion in both the FFP and PLT cohorts, whereas the majority of patients in the RBC cohort were not included in the FFP and PLT cohorts. The median age (IQR) of each of these adult cohorts was RBC 70 (54–79), FFP 66 (51–76) and PLT 62 (48–72).

Survival analysis

Overall survival was higher for the RBC group than the FFP and PLT groups (Fig. 1). RBC survival at 10 years was 36% (CI: 35% to 37%), whereas FFP and PLT survival was 30% (FFP CI: 29–32%, PLT CI: 28–32%).

As expected, survival decreased with increasing age (10 year log-rank $P < 0{\cdot}0001$), as shown in Fig. 2 for the RBC patients. Similar survival functions were found for the FFP and PLT groups. However, 10-year survival was lower for the younger patients in the PLT and FFP groups; 10-year survival for PLT patients aged 16–24 was 65% (CI 56–75%). For FFP patients, it was 74% (CI 65–81%), whereas for RBC patients it was 88% (CI 84–92%). These differences may be explained by differences in eCMG. A total of 38% of RBC 16–24 year olds were O&G patients, and only 8% had cancer. For 16–24-year-old FFP patients, 10% were O&G patients, and 7% had cancer. For

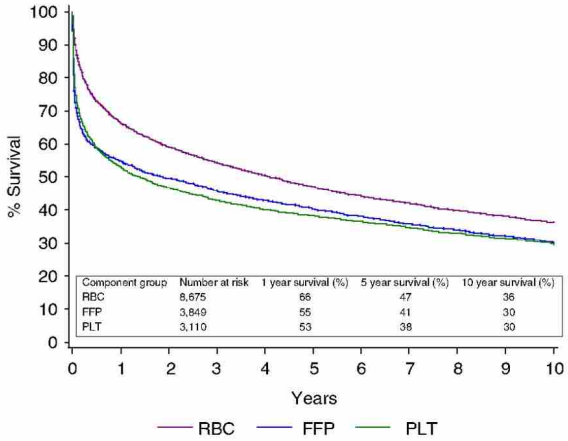


Fig. 1. Unadjusted survivor functions for patients in the RBC, FFP and PLT component groups.

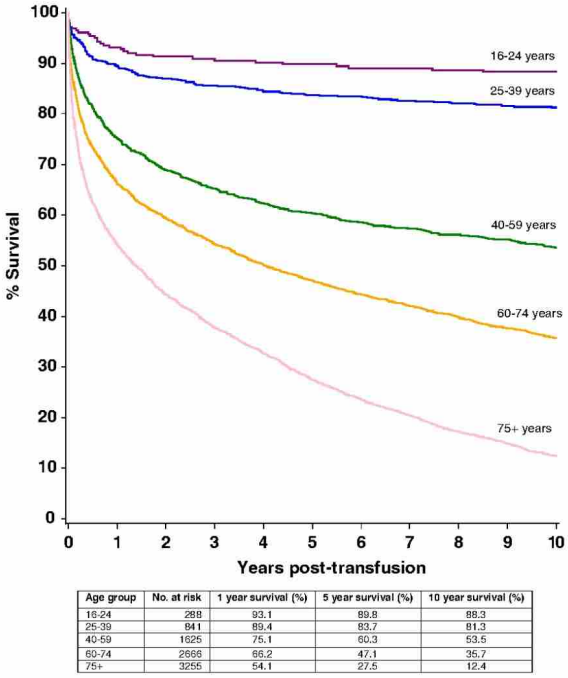
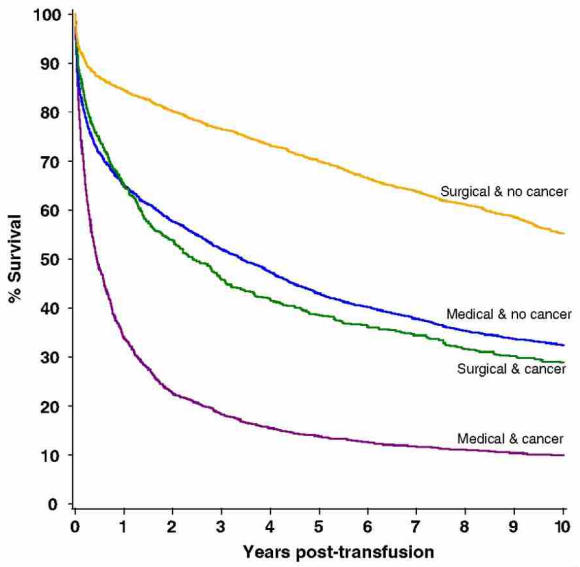


Fig. 2. RBC survivor functions stratified by age group.

16–24-year-old PLT patients, 6% were O&G patients, and 30% had cancer.

For RBC patients, survival was the lowest for patients diagnosed with cancer. Patients receiving a transfusion for medical rather than surgical reasons also had inferior survival. The 10-year survival for patients diagnosed with cancer who received a medical transfusion was 10% (CI 9% to 12%) compared to 55% (CI 53–57%) for patients who received a surgical transfusion and were not diagnosed with cancer (Fig. 3, 10-year log-rank $P < 0{\cdot}0001$). The survivor functions for the FFP and PLT groups were similar, although for PLT patients, the distinction between



Patient type	Number at risk	1 year survival (%)	5 year survival (%)	10 year survival (%)
Medical & cancer	1525	34.0	13.8	10.0
Medical & no cancer	3494	65.2	43.0	32.5
Surgical & cancer	807	65.0	36.8	29.0
Surgical & no cancer	3049	84.4	70.0	55.2

Fig. 3. RBC survivor functions stratified by cancer/no cancer and medical/surgical transfusion.

cancer diagnoses for the medical transfusion patients was less pronounced.

The survival functions for the RBC and PLT component groups stratified by eCMG are shown in Fig. 4. The survival functions for the FFP group were similar to those for the PLT group. The musculoskeletal and trauma eCMGs were combined in the FFP and PLT groups because of small numbers. For the FFP and PLT groups, the survival of the cardiac eCMG patients is the highest. The survival of the RBC cardiac patients is also high but the O&G survival is the highest.

Age group, eCMG, cancer and transfusion type were all found to be significantly associated with survival for all three component groups in the risk-adjusted analysis (Table 1). Older patients diagnosed with cancer who received a medical, rather than surgical, transfusion were found to have the highest mortality for all three component groups. For RBC patients, those with a vascular system eCMG and male patients also had higher risks. For FFP and PLT patients, gender was not found to be significant. For FFP patients, vascular system eCMG patients had the highest mortality and for PLT patients, those in the 'other' category had the highest (Table 1).

DISCUSSION

There are few studies that have attempted to define survival after transfusion in large cohorts (Vamvakas & Goldstein, 2002; Vamvakas, 2003; Kleinman *et al.*, 2004; Wallis *et al.*, 2004; Gauvin *et al.*, 2008; Kamper-Jorgensen *et al.*, 2008; Borkent-Raven *et al.*, 2011; Dorsey *et al.*, 2014). The majority have identified patients retrospectively and followed outcomes using population-based retrospective data sources (Tynell *et al.*, 2001; Kleinman *et al.*, 2004; Gauvin *et al.*, 2008; Kamper-Jorgensen *et al.*, 2008; Borkent-Raven *et al.*, 2011; Dorsey *et al.*, 2014). Borkent-Raven *et al.* (2011) looked back at clinical and transfusion data relating to 2 405 012 transfusions administered to adults and children in the Netherlands between 1996 and 2006. They followed the outcome of patients following individual component transfusion and found that 65·4% RBC, 70·4% FFP and 53·9% PLT were given to patients still alive after 1 year. The corresponding figures for 5 years were 46·4% RBC, 58·8% FFP, 39·3% PLT compared with our study in which prospective survival for the first 5 years between 2001 and 2005 was 47% RBC, 41% FFP and 38% PLT.

Kamper-Jorgensen *et al.* (2008) identified 1 118 261 transfusion recipients in Denmark, of whom 62% were aged 65 years or older at the time of their first registered transfusion. The 1-, 5- and 20-year survival was 73·7, 53·4 and 27·0%, respectively. Wallis *et al.* (2004) identified 2899 transfusion recipients in the North East of England in 1994. Overall survival at 5 years was 46·9% (95% CI, 45·1–48·7). Kleinman *et al.* (2004) retrospectively identified 6779 recipients transfused in 1995; 69% of patients were alive at 1 year and 46% were alive 5 years after transfusion.

Despite the differences in methodology and demographics, the headline figures of 60–70% 1-year and 50% 5-year survival are fairly consistent across all these studies. These figures are likely to predominantly reflect the survivors of red cell transfusions, as RBCs are much more commonly transfused than other components (Borkent-Raven *et al.*, 2010). Our study is the first national prospective study of transfusion recipients and has further explored those patients that receive other components. We have demonstrated that patients selected based upon either FFP or PLT transfusion exhibit considerably lower 1-, 5- and 10-year survival rates than those selected for RBC transfusion.

Several studies have shown that the majority of the post-transfusion deaths occurring within 10 years occurred within the first year (Kamper-Jorgensen *et al.*, 2008; Borkent-Raven *et al.*, 2011; Dorsey *et al.*, 2014). In our study, a similar pattern was observed with mortality of RBC 34%, FFP 45% and PLT 47% in the first year. Additional mortality across the subsequent 9 years was RBC 30%, FFP 25% and PLT 23%. This would appear to be in keeping with other studies that have shown raised mortality rates persisting to 10 years or more post-transfusion (Kamper-Jorgensen *et al.*, 2008; Borkent-Raven *et al.*, 2011). This ongoing raised mortality rate is likely to reflect the underlying medical conditions that led to transfusion, rather than the transfusions themselves.

In common with other countries reported, the EASTR-transfused population was skewed towards older age groups, with FFP and PLT recipients younger than RBC. We demonstrated that mortality following RBC transfusion increased with age, with risk-adjusted hazard ratio of death of 8·2 (6·9–9·2) for patients aged at least 75 years as compared with 16–39-year olds. Similar outcomes were noted in the Borkent–Raven age-related analysis. Young adults in the 16–39-year age group in the RBC cohort were noted to have the greatest likelihood of

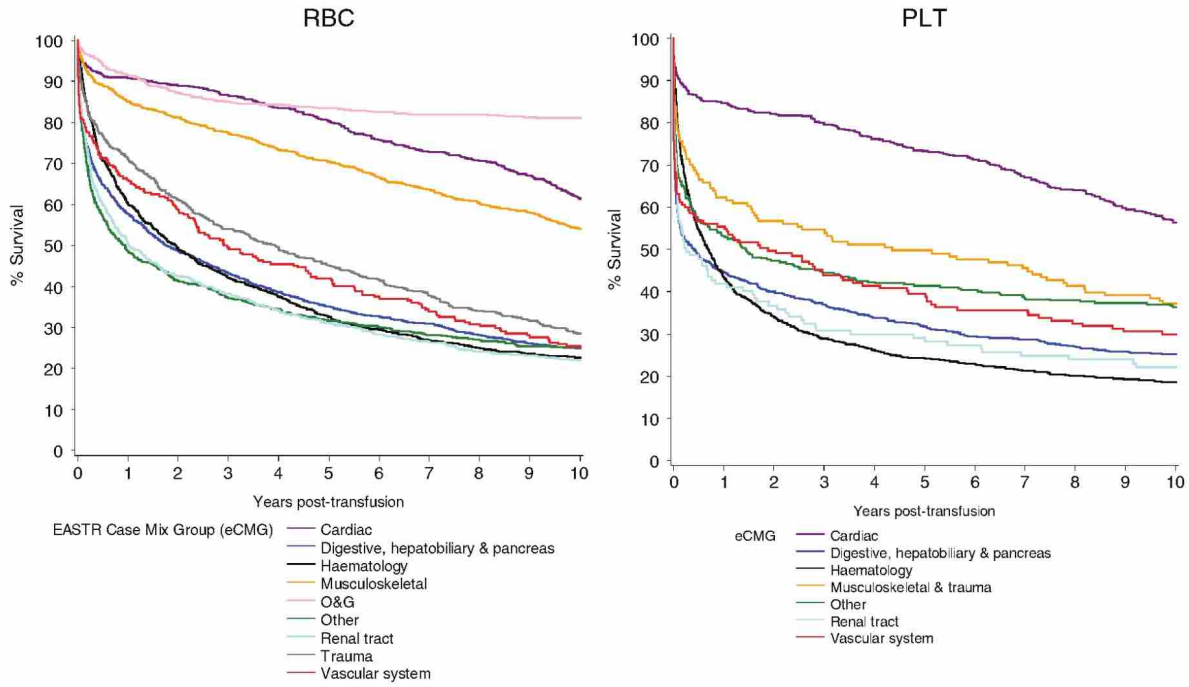


Fig. 4. RBC and PLT survivor functions stratified by EASTR case-mix group.

Table 1. Risk-adjusted modelling of the hazard of death after transfusion

		RBC			FFP			PLT		
Parameter		N	Hazard ratio (95% CL)	p-value	N	Hazard ratio (95% CL)	p-value	N	Hazard ratio (95% CL)	p-value
Age group	16–39	1028	1·0		465	1·0		450	1·0	
	40–59	1449	2·7 (2·2 to 3·2)	<0·0001	848	2·4 (2·0 to 2·8)	<0·0001	847	1·8 (1·6 to 2·2)	<0·0001
	60–74	2350	4·6 (3·8 to 5·4)		1203	3·5 (2·9 to 4·2)		981	3·2 (2·7 to 3·7)	
	75+	2846	8·2 (6·9 to 9·7)		989	5·2 (4·4 to 6·2)		582	5·2 (4·4 to 6·2)	
ECMG	Cardiac	579	1·0	<0·0001	470	1·0	<0·0001	479	1·0	<0·0001
	Haematology	1107	1·2 (1·0 to 1·4)		232	1·5 (1·2 to 1·8)		977	1·5 (1·2 to 1·8)	
	O&G	768	0·7 (0·5 to 0·8)		–	–	–	–	–	–
	Other[1]	4991	1·5 (1·3 to 1·7)		2550	1·6 (1·3 to 1·8)		1246	2·2 (1·9 to 2·6)	
	Vascular system	228	2·4 (2·0 to 3·0)		253	1·7 (1·4 to 2·1)		158	2·1 (1·7 to 2·6)	
Cancer?	No	5541	1·0	<0·0001	2726	1·0	<0·0001	1721	1·0	<0·0001
	Yes	2132	2·2 (2·1 to 2·4)		779	1·7 (1·5 to 1·8)		1139	1·5 (1·4 to 1·7)	
Transfusion type	Surgical	3656	1·0	<0·0001	1854	1·0	<0·0001	1193	1·0	<0·0001
	Medical	4017	2·3 (2·1 to 2·4)		1660	2·1 (1·9 to 2·3)		1667	2·0 (1·8 to 2·3)	
Gender	Female	4339	1·0	0·005	1505	1·0	0·2	1169	1·0	0·08
	Male	3334	1·1 (1·0 to 1·2)		2000	1·1 (0·9 to 1·1)		1691	1·1 (0·9 to 1·2)	

[1]Other includes digestive, hepatobiliary & pancreas, musculoskeletal, trauma and renal tract eCMGs.

long-term survival of any group, even compared with children under the age of 16 years in the EASTR study, for whom data has been published separately (Morley *et al.*, 2016). This young adult group was more likely to have been transfused for lower risk indications such as obstetrics and surgery, whereas children are more likely to be transfused for higher risk conditions such as perinatal problems or malignancy. Similar results were found in the Scandinavian (Kamper-Jorgensen *et al.*, 2008) study and in FFP recipients (not RBC or PLT) in the Dutch study (Borkent-Raven *et al.*, 2011).

Risk of death was also affected by the reason for transfusion. RBC recipients with cancer diagnoses were twice as likely to die in the study period, as were those receiving transfusions for non-surgical reasons. Of those patients who received an RBC index transfusion that was not related to surgery and who had a cancer diagnosis, 90% died during the 10-year study period. Recipients transfused for obstetric, cardiac and musculoskeletal diagnoses exhibited lower mortality than other recipient diagnostic groups throughout the 10-year study period.

It might be expected that survival following transfusion should have improved over recent decades, alongside the widespread improvements in medical care. Other studies have shown that survival may vary depending on the year in which transfusion occurred. Two studies (Kamper-Jorgensen *et al.*, 2008, Dorsey *et al.*, 2014) have previously shown increasing risk of early mortality in cohorts transfused in successive decades, possibly due to the changes in medical treatment and more stringent thresholds at which transfusion was prescribed (Dorsey *et al.*, 2014). In contrast, Tynell showed an improvement in 1-year survival between 1993 and 2000 in Sweden (Tynell *et al.*, 2001; Tynell *et al.*, 2005). Other studies have observed mortality for transfusions across many years (Vamvakas & Goldstein, 2002; Kamper-Jorgensen *et al.*, 2008; Borkent-Raven *et al.*, 2011; Dorsey *et al.*, 2014). Our study presents data from a single year, and should therefore not be influenced by changes in practice. There appears to have been little change in mortality after RBC transfusion in England between the North East regional study undertaken by Wallis *et al.* (2004) between 1994 and 1999, and this study commenced in 2001. As noted by Wallis *et al.* (2004), the failure to observe any improvement in mortality may reflect increasing use of transfusion for older patients and for medical conditions. It is also notable that there has been a significant reduction in RBC demand in England during the follow-up period of this study. The greatest reduction has occurred in individuals undergoing routine surgical procedures, who would be expected to have lower post-transfusion mortality. It is possible, therefore, that survival post-RBC transfusion may be lower than reported here for patients being transfused today. Recent work in the United States, however, has shown that reduction in RBC usage and utilisation of lower transfusion thresholds did not lead to any significant change in 30-day mortality for non-obstetric adult transfusion recipients (Roubinian *et al.*, 2014)

This study confirms that more than 50% of transfusion recipients die within 5 years of transfusion. This finding has been confirmed in other large European studies (Kamper-Jorgensen *et al.*, 2008; Borkent-Raven *et al.*, 2011), although survival in the Scandinavian cohort was fractionally higher. There are fewer US studies, and the cohort sizes are smaller, but there is a suggestion that the survival after transfusion is lower than in Europe, with the largest study (Kleinman *et al.*, 2004) showing 5-year survival of 46% and the most recent of 32% (Dorsey *et al.*, 2014). For UK RBC transfusions, those >60 years have greater than 50% mortality at 5 years (Wallis *et al.*, 2004). The EASTR study showed that the median age for RBC transfusion was 69 years (FFP 64 and PLT 59) before the paediatric cohort was removed (Wells *et al.*, 2009) suggesting that this is a comparable (and possibly slightly younger) cohort to those in the Netherlands and Scandinavia (Kamper-Jorgensen *et al.*, 2008; Borkent-Raven *et al.*, 2011) who have a median age of 67 and 69·9 years, respectively.

The EASTR study confirms that the age of English recipients and their expected survival following transfusion is comparable to that of other wealthy countries, where data are available. The majority of transfusion recipients die within 5 years of transfusion and by 10 years post-transfusion, around 70% are expected to die. It is difficult to ascertain from the available data any link between blood transfusion and excess mortality other than the risk attributable to the underlying conditions.

This study clearly demonstrates that long-term survival is common among younger recipients (especially those under the age of 40 years). This is especially true for RBC recipients. Young patients receiving multiple transfusions may therefore be at significant risk of infections with a long incubation period. Continued vigilance regarding TTI is therefore essential for this group as well as for the significant proportion of older recipients who are still alive at 10 years post-transfusion. There are some potential limitations to the use of patient survival data such as these to provide estimations of uncommon risks, such as long-term infection. Heavily transfused patients are less likely to survive because of their underlying illness; therefore survival by unit will generally be shorter than survival by patient. Use of patient survival data may; therefore, lead to overestimation of risk of infection. This study was undertaken at a time when variant CJD infections in the UK were at a peak, and we anticipate that this survival monitoring will contribute to the better understanding of risk in the context of this and future TTIs that have potential longer-term implications. Improving data collection in healthcare in the coming decades should allow us to derive detailed risk assessments for different patients receiving transfusions, allowing improved allocation of donated components.

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REFERENCES

Borkent-Raven, B.A., Janssen, M.P., van der, Poel, C.L., Schaasberg, W.P., Bonsel, G.J. & van, Hout, B.A. (2010) The PROTON study: profiles of blood product transfusion recipients in the Netherlands. *Vox Sanguinis*, **99**, 54–64.

Borkent-Raven, B.A., Janssen, M.P., van der, Poel, C.L., Schaasberg, W.P., Bonsel, G.J. & van, Hout, B.A. (2011) Survival after transfusion in the Netherlands. *Vox Sanguinis*, **100**, 196–203.

Dorsey, K.A., Moritz, E.D., Notari, E.P., Schonberger, L.B. & Dodd, R.Y. (2014) Survival of blood transfusion recipients identified by a

look-back investigation. *Blood Transfusion*, **12**, 67–72.

Gauvin, F., Champagne, M.A., Robillard, P., Le Cruguel, J.P., Lapointe, H. & Hume, H. (2008) Long-term survival rate of pediatric patients after blood transfusion. *Transfusion*, **48**, 801–808.

Hopewell, S., Omar, O., Hyde, C., Yu, L.M., Doree, C. & Murphy, M.F. (2013) A systematic review of the effect of red blood cell transfusion on mortality: evidence from large-scale observational studies published between 2006 and 2010. *BMJ Open*, **3**(5), e002154.

Jackson, B.R., Busch, M.P., Stramer, S.L. & AuBuchon, J.P. (2003) The cost-effectiveness of NAT for HIV, HCV, and HBV in whole-blood donations. *Transfusion*, **43**, 721–729.

Kamper-Jorgensen, M., Ahlgren, M., Rostgaard, K. *et al.* (2008) Survival after blood transfusion. *Transfusion*, **48**, 2577–2584.

Kent, J.T. & O'Quigley, J. (1988) Measures of dependence for censored survival data. *Biometrika*, **75**, 525–534.

Kleinman, S., Marshall, D., AuBuchon, J. & Patton, M. (2004) Survival after transfusion as assessed in a large multistate US cohort. *Transfusion*, **44**, 386–390.

Llewelyn, C.A., Wells, A.W., Amin, M. *et al.* (2009) The EASTR study: a new approach to determine the reasons for transfusion in epidemiological studies. *Transfusion Medicine*, **19**, 89–98.

Morley, S.L., Hudson, C.L., Llewelyn, C.A., Wells, A.W., Johnson, A.L. & Williamson, L.M. (2016) Transfusion in children: epidemiology and ten year survival of transfusion recipients. *Transfusion Medicine* doi: 10.1111/tme.12283. [Epub ahead of print].

Rohde, J.M., Dimcheff, D.E., Blumberg, N., Saint, S., Langa, K.M., Kuhn, L., Hickner, A. & Rogers, M.A. (2014) Health care-associated infection after red blood cell transfusion: a systematic review and meta-analysis. *JAMA*, **311**, 1317–1326.

Roubinian, N.H., Escobar, G.J., Liu, V. *et al.* (2014) Trends in red blood cell transfusion and 30-day mortality among hospitalized patients. *Transfusion*, **54** (10 Pt 2), 2678–2686.

Tynell, E., Norda, R., Shanwell, A. & Bjorkman, A. (2001) Long-term survival in transfusion recipients in Sweden, 1993. *Transfusion*, **41**, 251–255.

Tynell, E., Norda, R., Montgomery, S.M. & Bjorkman, A. (2005) Diagnosis and procedure-specific survival among transfusion of recipients in 1993 and 2000, Orebro County, Sweden. *Vox Sanguinis*, **88**, 181–188.

Vamvakas, E.C. (2003) Ten-year survival of transfusion recipients identified by hepatitis C lookback. *Transfusion*, **43**, 418–419.

Vamvakas, E.C. & Goldstein, R. (2002) Four-year survival of transfusion recipients identified by hepatitis C lookback. *Transfusion*, **42**, 691–697.

Wallis, J.P., Wells, A.W., Matthews, J.N. & Chapman, C.E. (2004) Long-term survival after blood transfusion: a population based study in the North of England. *Transfusion*, **44**, 1025–1032.

Wells, A.W., Llewelyn, C.A., Casbard, A. *et al.* (2009) The EASTR study: indications for transfusion and estimates of transfusion recipient numbers in hospitals supplied by the National Blood Service. *Transfusion Medicine*, **19**, 315–328.