The epidemiology of red cell transfusion

Barr, P., Donnelly, M., Morris, K., Parker, M., Cardwell, C., & Bailie, K. E. M. (2010). The epidemiology of red cell transfusion. Vox Sanguinis, 99(3), 239-250. DOI: 10.1111/j.1423-0410.2010.01349.x

Published in:
Vox Sanguinis

The International Journal of Transfusion Medicine
Vox Sanguinis

Vox Sanguinis (2010) **99**, 239–250

DOI: 10.1111/j.1423-0410.2010.01349.x

ORIGINAL PAPER

The epidemiology of red cell transfusion

P. J. Barr,[1] M. Donnelly,[1] K. Morris,[2] M. Parker,[3] C. Cardwell[1] & K. E. M. Bailie[4]

[1] *Centre for Excellence in Public Health, Queens University Belfast, Belfast, UK*
[2] *Northern Ireland Blood Transfusion Service, Belfast, UK*
[3] *Clinical Research Support Centre, Royal Hospitals, Belfast, UK*
[4] *West of Scotland Blood Transfusion Service, Glasgow, UK*

Vox Sanguinis

Background and Objectives Understanding of the clinical usage of red cells is limited despite its importance in transfusion practice improvement and planning for blood supply requirements. Previous studies have described red cell use based upon ICD and hospital discharge codes; however, such approaches are open to misclassification. This study addresses this limitation by undertaking an epidemiological analysis of red cell use using case note review.

Materials and Methods Patient, disease and contextual factors were extracted from the medical records of a randomly selected sample of hospital patients in Northern Ireland who received a red cell transfusion during 2005 (n = 1474).

Results Transfused patients received a total of 3804 units (median of two units per transfusion episode). Most transfusions occurred in a medical setting (71%). Patients undergoing treatment for gastrointestinal conditions were responsible for the majority of the demand (29% of transfusion episodes; 34% of red cell units). The presence of bleeding and abnormal tests of coagulation were associated with receiving larger transfusions (≥ 3 units), while patients undergoing orthopaedic surgery and those with a haemoglobin level over 7 g/dl had the lowest risk of receiving ≥ 3 units in any one transfusion episode.

Conclusion The majority of red cells are now prescribed in a medical setting. With an ageing population and increasing therapeutic interventions, the demand for blood is likely to increase despite efforts to reduce usage by eliminating inappropriate transfusions through education and behaviour change. The post-transfusion target (and therefore the number of units to transfuse) for any given clinical situation as well as guidance on a 'safe' transfusion threshold should be considered in future guidelines.

Received: 10 March 2010,
revised 21 April 2010,
accepted 25 April 2010,
published online 23 June 2010

Key words: blood supply requirements, blood transfusion, epidemiology, health services research.

Introduction

Knowledge of the clinical usage of red cells within the population it supplies is an important piece of information for transfusion services. Understanding this 'demand' can be helpful in matching supply to changing clinical demand, in facilitating discussion of the importance of appropriate red cell use in transfusion practice and in providing an appropriate denominator for haemovigilance data. Unfortunately, population-based data on red cell usage are currently limited [1–3]. The few studies available suggest that overall red cell usage as judged by the number of red cell units issued per 1000 of the population has been falling over recent years (Table 1) [4], driven mainly by changes in surgical practice [5]. Similar decreases have been observed in Finland and the USA [6]. Yet, future demand for red cells is likely to increase as a result of an ageing population and further advances in supportive care leading to increased

Correspondence: Paul Barr, School of Pharmacy, Queens University of Belfast, Belfast BT9 7BL, UK
E-mail: p.barr@qub.ac.uk

Table 1 Red cells issued per population in the UK and Ireland [4]

Red cells issued (per 1000 population)	Northern Ireland	Republic of Ireland	Scotland	England	Wales	Average
2004–2005	37·1	34·0	47·8	43·4	42·9	41·0
2005–2006	35·3	34·6	43·4	39·5	40·8	38·7
2006–2007	33·5	31·9	42·7	38·1	39·6	37·2
2007–2008	31·8	32·4	40·8	35·3	39·5	36·0
2008–2009	31·3	32·6	41·1	35·9	41·1	36·4

activity in a medical setting [3,7,8]. As can be seen in Table 1, a small average increase in red cell use in the UK has been noted for the period 2008/9, contrasting with the continued fall in red cell use reported for Northern Ireland, albeit at a much reduced rate. Other countries (France, Canada and Australia) have also recorded increases in the number of red cell issues per capita [6].

The observed reductions in red cell use in surgery may have been masking an increased demand from medical specialties [3]. With a likely plateau of efficiency having been reached in the surgical use of red cells, understanding the 'medical use' of red cells is increasingly imperative.

Published studies have attempted to address this issue by describing the fate of red cell units using information from hospital blood banks to indicate reason for transfusion, [2,3,9,10] or discharge codes to ascribe a clinical setting and a reason for transfusion [11]. Such approaches provide limited opportunity to examine the clinical scenario leading up to a transfusion and are prone to misclassification of patient, haematological and contextual factors associated with the transfusion [12].

Our study aimed to describe in detail (1) the types of patient that receive red cells in terms of their demographics, disease status, haematological parameters and area of clinical practice in which they were being treated; and (2) the quantity of red cell units typically used in a given transfusion episode, for a defined population served by a single national blood transfusion service.

Methods

Study sample

A random sample of all adults (≥ 18 years) who received an allogeneic red cell transfusion in Northern Ireland during 2005 was selected from each of the 11 hospital blood banks in Northern Ireland, which are supplied by a single regional blood transfusion service. Patients were identified from all of those issued with a red cell unit. The number of patients included from each hospital was proportionate to that hospital's annual red cell usage to avoid over-sampling within smaller hospitals. Only the first transfusion episode identified for any individual was included in the study, and thus, any patient could only appear once in the study population.

Transfusion episode

A transfusion episode was defined as the period between the first prescription of red cells and the receipt of those red cells by the patient. Where multiple units were prescribed for the same patient for the same condition, for example owing to acute bleeding, all units received were considered part of a single transfusion episode, up until the symptoms for that particular clinical episode had resolved.

Classification of patients

Patients were considered to be 'surgical' patients if they had undergone a surgical procedure within 2 weeks of a transfusion episode; all other patients were considered to be 'medical'. Only procedures that involved incision of the skin were classified as surgical; thus, patients undergoing endoscopy were not considered to be surgical cases. The presenting condition was defined as the primary condition being treated during the clinical episode in which the transfusion took place. Assignment of the primary condition was based on a detailed review of medical records, including discharge letters, pertaining to the episode of care in which the transfusion occurred. Co-morbidity was assessed through counting the number of co-morbid conditions present at the time of the admission in which the transfusion episode occurred [13,14].

The number of co-morbid conditions was summed for each patient. In an attempt to refine this 'measure' of co-morbidity and reflect the severity of the conditions present, we constructed the variable 'burden of disease' that was a count of the number of co-morbidities present that were associated with the most common causes of death in NI. Burden of disease was included in the regression analysis. Presenting conditions and co-morbid conditions were grouped using a systems approach to examine their impact of different clinical areas and the effect of different types of co-morbidity on blood use.

Data collection

Study data were abstracted from the hospital case notes and laboratory records of the selected patients using a study-specific case report form (CRF). The specified data items were chosen based on previously published studies of blood use and discussion with transfusion specialists (Table 2) [2,3,9,10]. A 10% sample of case notes and all CRFs were reviewed by a second abstractor (KB or KM), and any discrepancies were resolved by agreement. Laboratory parameters assigned for each case were those recorded as close to the transfusion decision point as possible, i.e. the last value recorded prior to transfusion.

Data analysis

Continuous data were summarized using a mean and standard deviation, or median and range, as appropriate. Categorical data were summarized using proportions across each category. Where appropriate, Pearson's chi squared test of independence was used to assess whether there was a statistical association between categorical variables; the Students *t*-test was used to investigate statistical differences between means; and Pearson's correlation coefficient was used to assess the strength of correlation between two variables. A Kruskal–Wallis test was used to compare the quantity of red cells transfused per episode (in four categories) between different groups of patients.

An initial unadjusted logistic analysis comparing episodes of ≤ 2 units of red cells with episodes ≥ 3 units (defined as larger transfusion) was conducted followed by a multiple logistic regression analysis, to identify those factors that influenced the quantity of red cells used per transfusion. Robust standard errors for estimates were used to account for clustering of patient characteristics within hospitals (Kirkwood & Sterne [15]; p 360). The level of statistical significance was taken to be $P < 0{\cdot}05$. All analyses were conducted using STATA® version 9.2 (StataCorp., College Station, TX, USA).

Table 2 Description of study variables

Variable	Variable definition/code/unit of measurement
Patient characteristics	
Gender	Male or female
Age	At the time of transfusion decision (years)
Weight	At the time of transfusion decision (kgs)
Anticoagulant medication	Within 1 week of transfusion
Chemotherapy or radiotherapy	Currently being received or not
Bleeding status	No bleeding; medical (non-surgical) bleeding; surgical blood loss; and additional (unexpected) peri-operative bleeding
Presenting condition	The primary condition being treated at the time of transfusion. The conditions were classified as: Gynaecology/obstetrics; cardiac; ear, nose throat (ENT); gastrointestinal; haematology; liver; metabolic/endocrine; neurological; musculoskeletal; respiratory; skin; urological; vascular; and other
Cancer-related treatment	Indicated whether the treatment a patient received was for cancer-related reasons
Co-morbidities	Co-existent medical conditions prior to transfusion (same categories as presenting condition)
Burden of disease score	A count of the total number of co-morbidities associated with mortality (according to the NI Mortality Statistics)
Clinical setting	
Patient setting	At the time of transfusion decision: inpatient or outpatient
MSBOS	Group & Screen; 2 units cross-matched; or ≥ 4 units cross-matched
Specialty and grade of health professional prescribing transfusion	Physician, surgeon, anaesthetist or obstetrician/gynaecologist. Consultant, Specialist Registrar, Senior House Officer or Junior House Officer
Patient management	Surgery within 2 weeks prior to transfusion (Surgical). No record of surgery in 2 weeks prior to transfusion (Medical)
Haematological and biochemical parameters	
Blood count	Last recorded result prior to transfusion. Includes Haemoglobin (g/dl)
Pretransfusion coagulation screen	Last recorded coagulation screen prior to transfusion. Includes prothrombin time (PT), activated partial thromboplastin time (APTT) and fibrinogen (Fib). Prolonged coagulation if either PT > 17 secs, APTT>45 secs or Fib < 1·5 secs; If not, coagulation not prolonged
Post-transfusion haemoglobin	Earliest recorded haemoglobin (g/dl) result post-transfusion.

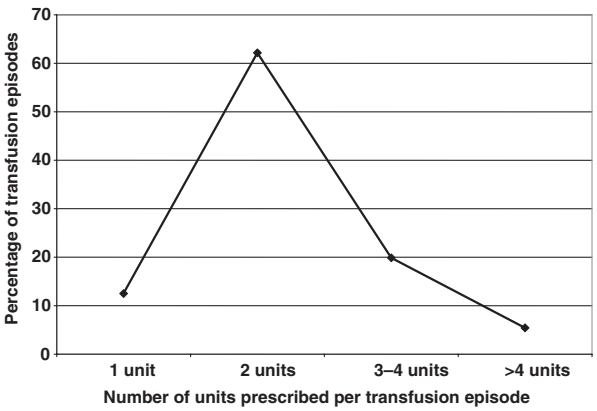

Fig. 1 Distribution of red cells prescribed per transfusion episode.

Results

A total of 1474 patients were included in the study. They received 3804 units of red cells between them, accounting for 6·1% of all red cells issued by NIBTS during 2005. A median of two units (range 1–28) was transfused per transfusion episode (Fig. 1). The mean change in haemoglobin per red cell unit transfused was 0·98 g/dl. Women tended to have a greater mean change in haemoglobin per unit transfused than men, 1·10 g/dl compared to 0·86 g/dl, respectively. This may be the result of differences in weight between men and women, 74·3 kg compared to 64·1 kg ($P < 0·0001$) respectively. The characteristics of the red cell transfusion recipients are summarized in Tables 3–7.

Data quality was generally good, although some missing data were encountered, particularly for weight, 38% (558/1474); post-transfusion haemoglobin, 13% (197/1474); and the specialty, 20% (292/1474) and grade, 14% (209/1474), of the prescribing clinician. The degree of missing information varied by specialty; weight information was more commonly missing among patients treated for gynaecological/obstetric conditions (47%), medical (44%) compared to surgical patients (25%) and patients in the oldest (48%) and youngest age groups (45%). Patients

Table 3 Characteristics of red cell recipients

Transfused patients (n = 1474)	Patients	Units transfused	Units transfused per transfusion episode*			
			1 unit	2 units	3–4 units	> 4 units
Patient parameters						
Gender			$P = 0·24$			
Male	689 (47%)	1833 (48%)	78 (11%)	432 (63%)	133 (19%)	45 (7%)
Female	785 (53%)	1971 (52%)	107 (14%)	484 (62%)	160 (20%)	35 (4%)
Age groups (years)			$P \leq 0·001$			
18 ≥ , years, < 45	195 (13%)	584 (15%)	12 (6%)	123 (63%)	42 (22%)	18 (9%)
45 ≥ , years, < 60	236 (16%)	642 (17%)	21 (9%)	150 (64%)	53 (23%)	12 (5%)
60 ≥ , years, < 70	287 (20%)	709 (19%)	38 (13%)	185 (65%)	52 (18%)	12 (4%)
70 ≥ , years, < 80	383 (26%)	965 (25%)	54 (14%)	250 (65%)	58 (15%)	21 (6%)
80 ≥ years	373 (25%)	904 (24%)	60 (16%)	208 (56%)	88 (24%)	17 (5%)
Weight Groups (kg)[a]			$P = 0·05$			
< 55 Kgs	180 (20%)	383 (17%)	30 (17%)	123 (68%)	22 (12%)	5 (3%)
55 ≥ , Kgs, < 65	210 (23%)	514 (23%)	27 (13%)	126 (60%)	48 (23%)	9 (4%)
65 ≥ , Kgs, < 75	203 (22%)	494 (23%)	30 (15%)	122 (60%)	43 (21%)	8 (4%)
75 ≥ , Kgs, < 85	163 (18%)	385 (18%)	21 (13%)	113 (69%)	21 (13%)	8 (5%)
85 ≥ Kgs	160 (17%)	423 (19%)	20 (13%)	98 (61%)	30 (19%)	12 (7%)
Anticoagulant medications			$P \leq 0·001$			
Yes	846 (57%)	2049 (54%)	139 (16%)	509 (60%)	156 (19%)	42 (5%)
No	628 (43%)	1755 (46%)	46 (7%)	407 (65%)	137 (22%)	38 (6%)
Current chemotherapy/radiotherapy			$P = 0·56$			
Yes	157 (11%)	379 (10%)	6 (4%)	126 (80%)	23 (15%)	2 (1%)
No	1317 (89%)	3425 (90%)	179 (14%)	790 (60%)	270 (21%)	78 (6%)
Bleeding status			$P < 0·001$			
Medical: no bleeding	617 (42%)	1358 (36%)	49 (8%)	445 (72%)	117 (19%)	6 (1%)
Medical: bleeding	429 (29%)	1352 (36%)	41 (10%)	244 (57%)	103 (24%)	41 (10%)
Surgical: bleeding	323 (22%)	709 (19%)	83 (26%)	177 (55%)	50 (15%)	13 (4%)
Surgical: additional peri-operative bleeding	105 (7%)	385 (10%)	12 (11%)	50 (48%)	23 (22%)	20 (19%)

[a]Missing values. *Kruskal-Wallis test comparing the distribution of red cells transfused (in four categories) between groups of patients

Table 4 Setting parameters of red cell transfusion recipients

Transfused patients (*n* = 1474)	Patients	Units transfused	Units transfused per transfusion episode*			
			1 unit	2 units	3–4 units	> 4 units
Setting parameters						
Patient management			$P < 0{\cdot}001$			
Medical	1046 (71%)	2710 (71%)	90 (9%)	689 (66%)	220 (21%)	47 (4%)
Surgical	428 (29%)	1094 (29%)	95 (22%)	227 (53%)	73 (17%)	33 (8%)
MSBOS			$P < 0{\cdot}001$			
G&S	194 (45%)	442 (40%)	51 (26%)	108 (56%)	25 (13%)	10 (5%)
2 units cross-matched	189 (44%)	487 (45%)	37 (20%)	100 (53%)	38 (20%)	14 (7%)
≥ 4 units cross-matched	45 (11%)	165 (15%)	7 (16%)	19 (42%)	10 (22%)	9 (20%)
Patient setting			$P = 0{\cdot}17$			
Inpatient	1316 (89%)	3469 (91%)	179 (14%)	783 (59%)	273 (21%)	80 (6%)
Outpatient	158 (11%)	335 (9%)	6 (4%)	133 (84%)	20 (13%)	0 (–)

*Kruskal-Wallis test comparing the distribution of red cells transfused (in four categories) between groups of patients

Table 5 Red cell use by medical and surgical specialities

Transfused Patients (*n* = 1474) Management presenting condition	No. of patients (% by management)	Oncology-related condition (% by condition)	Red cell units used (% by management)	Units transfused per episode*			
				1 unit	2 units	3–4 units	> 4 units
Medical (*n* = 1046)				$P = 0{\cdot}04$			
Gastrointestinal	341 (33%)	75 (22%)	1034 (38%)	35 (10%)	191 (56%)	85 (25%)	30 (9%)
Haematology	222 (21%)	127 (57%)	529 (20%)	9 (3%)	163 (73%)	47 (21%)	3 (1%)
Urological	89 (9%)	41 (46%)	192 (7%)	8 (9%)	67 (75%)	12 (13%)	2 (2%)
Respiratory	85 (8%)	42 (49%)	196 (7%)	4 (5%)	63 (74%)	16 (19%)	2 (2%)
Gynaecology/obstetric	76 (7%)	42 (55%)	174 (6%)	2 (3%)	55 (72%)	19 (25%)	0 (–)
Cardiac	56 (5%)	0 (–)	127 (5%)	4 (22%)	42 (75%)	9 (16%)	1 (2%)
Musculoskeletal	51 (5%)	9 (18%)	116 (4%)	9 (18%)	29 (57%)	12 (24%)	1 (2%)
Vascular	31 (3%)	3 (10%)	90 (3%)	4 (13%)	19 (61%)	4 (13%)	4 (13%)
Neurological	21 (2%)	1 (5%)	49 (2%)	7 (33%)	10 (48%)	3 (14%)	1 (5%)
Liver	21 (2%)	4 (19%)	44 (2%)	2 (9%)	17 (81%)	2 (10%)	0 (–)
Metabolic/endocrine	17 (2%)	5 (29%)	41 (2%)	4 (22%)	8 (44%)	6 (33%)	0 (–)
Skin	10 (1%)	1 (10%)	21 (1%)	0 (–)	9 (90%)	1 (10%)	0 (–)
ENT	3 (0·3%)	0 (–)	6 (0·2%)	0 (–)	3 (100%)	0 (–)	0 (–)
Other	22 (2%)	5 (23%)	91 (3%)	2 (9%)	13 (59%)	4 (18%)	3 (14%)
Oncology-related condition (total)		355 (34%)	806 (30%)	19 (5%)	270 (76%)	64 (18%)	2 (1%)
Surgical (*n* = 428)				$P < 0{\cdot}001$			
Musculoskeletal	141 (33%)	0 (–)	275 (25%)	46 (33%)	77 (55%)	12 (9%)	6 (4%)
Gastrointestinal	88 (21%)	37 (42%)	250 (23%)	12 (14%)	51 (58%)	17 (19%)	8 (9%)
Cardiac	53 (12%)	0 (–)	155 (14%)	13 (25%)	18 (34%)	18 (34%)	4 (8%)
Vascular	51 (12%)	0 (–)	146 (13%)	12 (24%)	25 (49%)	9 (18%)	5 (10%)
Gynaecology/obstetric	51 (12%)	10 (20%)	157 (14%)	4 (8%)	31 (61%)	11 (22%)	5 (10%)
Urological	21 (5%)	15 (71%)	54 (5%)	4 (19%)	11 (52%)	2 (10%)	4 (19%)
Neurological	7 (2%)	2 (29%)	14 (1%)	2 (29%)	4 (57%)	1 (14%)	0 (–)
Respiratory	3 (1%)	0 (–)	7 (1%)	0 (–)	2 (67%)	1 (33%)	0 (–)
Metabolic/endocrine	5 (1%)	3 (60%)	9 (1%)	1 (20%)	4 (80%)	0 (–)	0 (–)
Skin	4 (1%)	0 (–)	10 (1%)	0 (–)	3 (75%)	1 (25%)	0 (–)
Other	4 (1%)	0 (–)	17 (2%)	1 (25%)	1 (25%)	1 (25%)	1 (25%)
Oncology-related condition (total)		67 (16%)	166 (15%)	15 (22%)	37 (55%)	9 (13%)	6 (9%)

*Kruskal-Wallis test comparing the distribution of red cells transfused (in four categories) between groups of patients

Table 6 Patient characteristics by presenting condition

Presenting condition	Medical:surgical	Male:female	Age; years (range)	Haemoglobin; g/dl (range)	Burden of disease (range)
Gastrointestinal	341:88	227:202	72 (23–95)	7·8 (4–16)	3 (0–7)
Cardiac	56:53	62:47	75 (29–90)	7·5 (5·3–13·1)	3 (1–6)
Haematology	222:0	111:111	73 (26–91)	8·3 (4·4–10·7)	2 (0–6)
Vascular	31:51	50:32	75 (20–94)	8·1 (5·1–15·5)	3 (0–6)
Respiratory	85:3	43:45	67 (28–92)	8·2 (4·5–9·9)	3 (0–7)
Musculoskeletal	51:141	63:129	76 (26–96)	7·9 (5·1–13·2)	2 (0–6)
Urological	89:21	75:35	73 (37–93)	8·2 (4·4–13·5)	3 (0–6)
Gynaecology/obstetrics	76:51	0:127	41 (20–87)	7·8 (4·7–13·8)	1 (0–6)
Other (including: liver, ENT, skin, neurological, metabolic)	95:20	57:58	65 (20–94)	7·6 (4·1–12·4)	2 (0–7)
Oncology-related admission					
Yes	355:67	222:200	67 (19–100)	8·3 (4·8–13·5)	2 (1–7)
No	691:361	466:586	73 (21–94)	7·7 (2·3–16)	2 (0–7)

Table 7 Haematological parameters of red cell transfusion recipient

Transfused patients (n = 1474)	Patients	Units transfused	Units transfused per transfusion episode*			
			1 unit	2 units	3–4 units	> 4 units
Haematological parameters						
Pretransfusion Hb (g/dl)			$P < 0{\cdot}001$			
< 7 g/dl	295 (20%)	1020 (27%)	13 (4%)	113 (38%)	132 (45%)	37 (13%)
7 g/dl ≥, Hb, < 8 g/dl	476 (32%)	1189 (31%)	52 (11%)	311 (65%)	96 (20%)	17 (4%)
8 g/dl ≥, Hb, < 9 g/dl	433 (29%)	990 (26%)	75 (17%)	300 (69%)	45 (10%)	13 (3%)
9 g/dl ≥, Hb, < 10 g/dl	190 (13%)	386 (10%)	33 (17%)	143 (75%)	11 (6%)	3 (2%)
≥ 10 g/dl	78 (5%)	215 (6%)	12 (15%)	47 (60%)	9 (12%)	10 (13%)
Post-transfusion Hb[a]			$P < 0{\cdot}001$			
< 10 g/dl	560 (44%)	1335 (41%)	112 (20%)	321 (57%)	99 (18%)	28 (5%)
≥ 10 g/dl, Hb, < 11 g/dl	339 (27%)	843 (26%)	42 (12%)	220 (65%)	62 (18%)	15 (4%)
≥ 11 g/dl, Hb, < 12 g/dl	206 (16%)	597 (18%)	10 (5%)	133 (65%)	47 (23%)	16 (8%)
≥ 12 g/dl	172 (13%)	516 (16%)	7 (4%)	107 (62%)	45 (26%)	13 (8%)
Prolonged coagulation[a]			$P = 0{\cdot}002$			
Yes	300 (36%)	1412 (50%)	42 (14%)	156 (52%)	65 (22%)	37 (12%)
No	533 (64%)	1435 (50%)	61 (11%)	338 (63%)	102 (19%)	32 (6%)

[a]Missing values. *Kruskal-Wallis test comparing the distribution of red cells transfused (in four categories) between groups of patients

treated for cardiac conditions had a notably lower proportion of missing weight information (10%). A large proportion of patients with missing post-transfusion haemoglobin were those treated for haematological (34%) or gynaecological/obstetric conditions (21%) and those treated in the outpatient setting (65%). The proportion of missing grade and specialty information regarding prescribing clinician was similar among specialties, with the exception of haematology, where very little information was missing, 8% and 2%, respectively.

The majority of transfusions were undertaken as inpatient episodes (89%), and a small majority of transfusion recipients were women (53%). The mean age at the time of transfusion was 67·1 years (SD 17·3), range 19–100 years, with no statistically significant difference between men and women. Two-thirds of transfusion recipients (68%) were aged 60 years or over. The number of co-morbidities present among transfusion recipients had a moderate positive correlation with age ($r = 0{\cdot}46$; $P < 0{\cdot}0001$), with a mean of four co-morbidities recorded (SD 2·0) per patient.

Given the large number of individual co-morbidities recorded, only classes of co-morbidity were grouped for analysis. However, it was possible to examine the relationship between individual co-morbidities (e.g. hypertension) and transfusion. The most common co-morbidities recorded were gastrointestinal conditions (45%; 665/1474); cardiac conditions (39%; 579/1474); cancer (38%; 560/1474); hypertension (32%; 476/1474); musculoskeletal conditions

(31%; 459/1474); and vascular conditions (26%; 390/1474).

Of the transfused population, 71% (1046/1474) were classified as 'medical' patients (Table 4). Medical patients were older than surgical patients, 68 (SD 16·9) and 65 (SD 18·0) years old, respectively ($P = 0·003$); however, there were no significant differences in the gender or pretransfusion haemoglobin levels among medical and surgical patients. The most common presenting conditions were in the gastrointestinal (29%; 429/1474), haematological (15%; 222/1474) and musculoskeletal (13%; 192/1474) categories. The pattern of presenting conditions differed between medical and surgical patients (Table 5). Among medical patients, gastrointestinal (33%; 341/1046) or haematological problems (21%; 222/1046) were most commonly recorded, whereas musculoskeletal (33%; 141/428), and gastrointestinal problems (21%; 88/428) were most prevalent among surgical patients. Cancer was the primary condition being treated in 34% (355/1046) of medical and 16% (67/428) of surgical patients, accounting for 30% (806/2710) and 15% (166/1094) of transfused units within each group, respectively. The characteristics of patients, by presenting condition, are highlighted in Table 6.

Almost two-thirds (61%) of transfusion recipients had a haemoglobin value between 7 and 9 g/dl (Table 7). A small minority (5%) were transfused with a haemoglobin value > 10 g/dl. A higher proportion of patients in this group had documented bleeding prior to transfusion, 83% (65/78 patients) compared to 57% (791/1394 patients) with a pretransfusion haemoglobin below 10 g/dl ($P < 0·001$). Also, a higher proportion of patients transfused with a haemoglobin above 10 g/dl presented with gastrointestinal (27/78 patients; 35%), gynaecological (14/78 patients; 18%) and vascular (12/78 patients; 15%) conditions, in comparison to patients with a pretransfusion haemoglobin below 10 g/dl, 402/1394 (29%), 113/1394 (8%) and 70/1394 (5%), respectively ($P < 0·001$).

The mean pretransfusion haemoglobin was 8·0 g/dl (SD 1·4); range 4–16 g/dl, and the mean post-transfusion haemoglobin was 10·3 g/dl (SD 1·5); range 5·6–15·6 g/dl. Pretransfusion haemoglobin was found to differ significantly ($P < 0·001$) depending on the presenting condition; patients being treated for cardiac conditions had the lowest pretransfusion haemoglobin (7·5 g/dl), while patients having treatment for haematological or oncology conditions had the joint highest median pretransfusion haemoglobin (8·3 g/dl) (Table 6). Just over half (57%) were taking medications that could affect some aspect of coagulation. Of the 833 patients in whom a formal laboratory test was undertaken, 36% showed evidence of aberrant coagulation (Table 2).

For those transfusion episodes where the prescribing clinician was recorded, consultants (39%; 456/1182) and senior house officers (SHOs) (31%; 363/1182) were responsible for the majority of transfusion decisions. The majority of consultants were physicians (50%; 229/454) with anaesthetists and surgeons accounting for 26% (120/454) and 21% (93/454) of consultants, respectively. SHOs consisted mainly of physicians (65%; 225/349) followed by surgeons (25%; 88/349). On 1% (18/1474 episodes) of occasions, multiple prescribers were present and it was not clear who initiated the transfusion episode. In these episodes, the patients tended to receive larger transfusions (ranging from five units to 28 units).

Quantity of red cell units per transfusion episode

There were statistically significant variations across different patient groups in the quantity of red cells used per transfusion episode (Tables 3–7). Single-unit transfusions were most common among surgical patients (22%; 95/428), those patients over 80 years of age (16%; 60/373) and patients with a pretransfusion haemoglobin level between 8 and 10 g/dl (17%; 108/623). Two-unit transfusions were common among medical patients being treated for cancer (76%; 270/355), particularly if they were undergoing chemotherapy or radiotherapy (80%; 126/157).

The highest proportions of larger transfusions (three or more units) were more commonly found in the youngest age group (31%; 60/195); among patients with additional perioperative bleeding (41%; 43/105) or medical (non-surgical) bleeding (34%; 144/429); those with abnormal coagulation (48%; 144/300); and those with a haemoglobin level below 7 g/dl (57%; 169/295). Interestingly, a significant number of patients transfused with a recorded haemoglobin level over 10 g/dl also received a high proportion three or more units (24%; 19/78), and as previously mentioned, these patients tended to be bleeding prior to transfusion.

A multiple logistic regression analysis was conducted to identify factors associated with patients receiving larger transfusions, defined as ≥ 3 units transfused in one episode ($n = 373$ patients). In the unadjusted logistic regression analysis, several variables demonstrated an association with larger transfusions; however; only five parameters were found to be independently associated with the quantity of red cells transfused (Table 8).

The presence of bleeding in a medical setting (OR 1·50; 95% CI 1·03–2·18), additional peri-operative bleeding in the surgical setting (OR 2·47 (95% CI 1·20–5·11) and abnormal coagulation (OR 1·68; 95% CI 1·29–2·19) were associated with larger transfusions. Patients being treated for a musculoskeletal condition (mostly orthopaedic surgery, $n = 151$, 73%) (OR 0·53; 95% CI 0·36–0·78) and those with haemoglobin level above 7 g/dl (OR 0·52 per unit rise in haemoglobin; 95% CI 0·43–0·62) were at the lowest risk of receiving ≥ 3 units of red cells.

Table 8 Factors associated with the transfusion of ≥ 3 units of red cells

Variable	Unadjusted odds ratio (95% CI)	*P*-value	Adjusted odds ratio (95% CI)	*P*-value
Age				
Per year increase	1·00 (0·98–1·00)	0·44	1·00 (0·99–1·01)	0·29
Gender				
Male (Ref Cat.)	1·00	–	1·00	–
Female	0·95 (0·70–1·27)	0·71	0·89 (0·69–1·14)	0·34
Pretransfusion haemoglobin				
< 7 g/dl (Ref Cat)	1·00	–		
7g/dl ≥, Hb, <8g/dl	0·23 (0·20–0·28)	< 0·001	0·23 (0·20–0·26)	< 0·001
8g/dl ≥, Hb, <9g/dl	0·11 (0·07–0·20)	< 0·001	0·11 (0·06–0·20)	< 0·001
9g/dl ≥, Hb, <10g/dl	0·06 (0·03–0·11)	< 0·001	0·06 (0·03–0·12)	< 0·001
≥ 10 g/dl	0·24 (0·12–0·47)	< 0·001	0·24 (0·13–0·42)	< 0·001
Patient bleeding status[b]				
Medical: no bleeding (Ref Cat.)	1·00	–	1·00	–
Medical: bleeding	2·03 (1·56–2·64)	< 0·001	1·50 (1·03–2·18)	0·03
Surgical: bleeding	0·97 (0·54–1·75)	0·93	0·72 (0·44–1·18)	0·19
Surgical: additional peri-operative bleeding	2·79 (1·65–4·72)	< 0·001	2·47 (1·20–5·11)	0·001
Coagulation status				
Normal (Ref Cat.)	1·00	–	1·00	–
Prolonged	1·53 (1·23–1·91)	< 0·001	1·68 (1·29–2·19)	< 0·001
Not recorded	0·81 (0·55–1·19)	0·28	1·05 (0·71–1·57)	0·80
Chemotherapy/radiotherapy				
No (Ref Cat.)	1·00	–	1·00	–
Receiving chemotherapy/radiotherapy	0·53 (0·34–0·81)	0·003	0·97 (0·62–1·52)	0·90
Cancer-related treatment				
No (Ref Cat.)	1·00	–	1·00	–
Receiving treatment for cancer	0·62 (0·52–0·73)	< 0·001	0·96 (0·70–1·33)	0·82
Presenting condition				
Gastrointestinal (Ref Cat.)	1·00	–	1·00	–
Gynaecology	0·79 (0·43–1·43)	0·43	0·74 (0·36–1·49)	0·39
Haematology	0·60 (0·34–1·06)	0·08	0·88 (0·52–1·48)	0·63
Cardiac	0·86 (0·43–1·70)	0·66	0·82 (0·41–1·66)	0·59
Respiratory	0·57 (0·26–1·24)	0·16	0·77 (0·34–1·78)	0·55
Musculoskeletal	0·40 (0·27–0·59)	< 0·001	0·53 (0·36–0·78)	0·001
Urological	0·46 (0·21–0·98)	0·05	0·57 (0·30–1·09)	0·09
Vascular	0·76 (0·49–1·17)	0·21	0·73 (0·46–1·15)	0·17
Other	0·54 (0·31–0·95)	0·03	0·47 (0·27–0·81)	0·006
Burden of disease				
Per increase in co-morbidity	0·92 (0·84–1·03)	0·18	0·89 (0·77–1·02)	0·08

Adjusted for clustering by hospitals.

[b]Owing to potential collinearity with bleeding status, patient management (medical/surgical) was not included in this analysis. Bleeding status provided a more detailed breakdown of the medical/surgical split and was therefore preferred.

Discussion

Ensuring the efficient management of the supply and use of red cells has become a high priority for transfusion services to ensure that clinical needs continue to be met. Identifying the key characteristics of the transfused population is an important issue for those in the transfusion services, in the context of business planning to meet expected demand in the light of potential changes in the prevalence of the population characteristics associated with red cell use; and in clinical practice, in highlighting areas of high demand where encouraging appropriate use of blood is of particular concern.

The clinical use of red cells

A major finding of our study was the much larger proportion of transfusion activity occurring within the medical domain (71%) in comparison to the surgical domain (29%). This confirms recent observations made in other regions of

the UK [3,8,10,16], although the absolute proportion in our study was larger. In our study, only patients undergoing a surgical procedure within 2 weeks prior to transfusion were considered as surgical patients. Differences in the definition of what constitutes a medical or surgical transfusion may account for the conflicting findings of other studies [9,17,18]. Other potential explanations for the different medical/surgical split across studies may include different transfusion practices, medical care or population structures. Alternatively, the variation may be an indication of the changing pattern of blood use within the different clinical areas over time.

The conditions most commonly represented among transfused patients were similar to those reported previously, namely gastrointestinal (29%), haematological (15%) and musculoskeletal (13%) conditions [3,10,19]. Some 29% of the transfused patients in our study were being treated for cancer, including haematological malignancy; a large number were medical patients (355/422 patients). This is consistent with the findings of previous investigators who noted that patients suffering from bone marrow disorders and other malignancies were significant users of red cells [20,21].

Similar to previous studies, older age and low haemoglobin level were associated with the use of red cell transfusion [2,3,7,10,19,20]. More frequent transfusion among the elderly may be a consequence of higher levels of co-morbidity linked to an impaired ability to tolerate anaemia. Another contributing factor may be the perceived benefit/risk trade-off when considering transfusion in this age group. Some of the risks associated with transfusion, such as transfusion-transmitted infections, have long latent periods and as a result may be of less concern in those with a shorter life expectancy. For younger patients, the avoidance of potential longer term risks may encourage the avoidance of transfusion [22].

The observed reduction in transfusion among the over 80 year olds has been reported previously [17] and may be a result of the lesser exposure of such patients to intensive treatment or complex procedures requiring red cell support. Alternatively, the over 80s may be a group of 'fit' survivors in whom medical intervention in general is less likely.

Studies to date have tried to describe red cell use by examining the fate of red cell units or by describing the transfusion experience of defined groups of patients, most commonly those undergoing a particular surgical procedure. Many have classified patients and/or transfusion episodes using hospital discharge codes [11] or forms completed in the blood bank following a transfusion episode [2,3,9,10]. However, such definitions are open to misclassification; for example, in one study [9], 12·8% of the study sample could have been placed in either the medical or surgical domain. Furthermore, as there is little or no clinical or laboratory information available for inclusion in an analysis, such studies cannot comment on the timing of transfusion or provide an accurate description of the clinical context in which the transfusion episode took place [11]. Using the red cell unit as the unit of analysis provides an inventory of usage, among high and low users in different specialities or geographies. However, to examine the patient-related factors that are associated with red cell use and thus the drivers of demand requires the unit of analysis to be the patient or clinical episode, as adopted in our study.

Quantity of red cells used per transfusion episode

A two-unit transfusion was the most commonly encountered scenario in our study (62%). The practice of transfusing pairs of red cell units is widely reported, despite some guidelines highlighting the unnecessary risk to patients of prescribing multiple units (particularly pairs of red cells) based on habit and not on evidence or patient need [23]. It has been suggested that best practice is to reassess the patient's condition after transfusion of each unit before prescribing further units [24–26]. However, British Committee for Standards in Haematology [27] (BCSH) recommends transfusing two units during a transfusion episode.

Grey & Finlayson [25] found that a single unit of red cells could increase the haemoglobin level by 1·0 g/dl or more (depending on bleeding status, patient size, dehydration and haemoglobin concentration of red cells). Therefore, they recommended the use of single-unit transfusions as a means of both reducing red cell use and reducing inappropriate practice. However, patient management pathways may not always facilitate such an approach, particularly in an outpatient setting. In our study, the proportion of two-unit transfusions was particularly high among patients treated for cancer or haematological conditions. Such patients may be transfused to achieve an adequate haemoglobin level that will sustain them until their next treatment or review appointment.

In keeping with this interpretation, single-unit transfusion episodes were more common among surgical patients and the elderly, groups that are largely inpatient based. In the elective surgical setting, blood losses are likely to be controlled [5], with less need for 'top up' transfusion as a consequence. An additional factor in the older group is the greater likelihood of associated co-morbidity resulting in a more limited ability to tolerate the 'fluid challenge' of a larger transfusion. Furthermore, the capacity for tolerance of anaemia and haemoglobin recovery is likely to be greater in younger patients, making the one-unit transfusion unnecessary.

Interestingly, the only specialty to be associated with the quantity of red cell used per transfusion episode appeared

to be musculoskeletal; patients treated in this specialty were much less likely to receive a transfusion of three or more units. Musculoskeletal patients were mainly surgical (141/192 patients; 73%) and as previously mentioned, surgical patients had a high proportion of single-unit transfusions (95/428 patients; 22%). In addition, the operation of strict transfusion protocols within orthopaedic units in our study may have contributed to this finding. A miscellaneous group with 'other' conditions was included to avoid losing data from the statistical model. This group also appeared to have a reduced risk of larger transfusions; however, given the heterogeneity of this group, clinically useful conclusions cannot be drawn.

Transfusions of three units of red cells or more were more common among younger patients and those with a haemoglobin level below 7 g/dl and above 10 g/dl. Following the multiple logistic regression analysis, the situations found to be independently associated with an increased risk of receiving a transfusion of three or more units were the presence of abnormal coagulation test results and active bleeding either in a medical setting or as 'unexpected' bleeding during surgical procedures. A common factor is likely to be the volume of blood loss and the less 'stable' condition of the patient during such clinical events.

It is likely to be difficult, and perhaps harmful, to implement strict transfusion protocols, such as those used in orthopaedic surgery, aimed at reduction in red cell use in 'unstable' clinical settings, such as among medical patients with bleeding. Yet, such patients account for a significant proportion of red cell units transfused (1352/3804 units; 36%), so it is important to understand how and why red cells are being used in these circumstances if effective and efficient practice is to be encouraged. Such approaches are currently lacking in transfusion research, yet there is a wealth of psychological literature regarding clinical decision-making, which may be of use in this area [28,29]. Furthermore, research currently being undertaken in the UK and Canada may shed light on the psychology of clinical decision-making in transfusion medicine [30,31].

Strengths and limitations

The main strength of the approach taken in our study was the use of individual chart review to provide richness of detail surrounding transfusion episodes and thus reduces the risk of misclassification of patient or clinical factors. However, this approach is time-consuming and can lead to a time lag in the publication of results. Nevertheless, our results are likely still to be valid and to provide useful insights into red cell use, as transfusion guidelines have remained unchanged in Northern Ireland and the UK. The implementation of electronic medical records has been touted as a solution to providing real-time and detailed inpatient information, yet its implementation is still limited because of the presence of several barriers, such as financial pressure and resistance from clinicians [32].

Reliably identifying a denominator for transfused patients and those at risk of transfusion is difficult. Current systems within hospitals vary and do not always allow the ready identification of transfused patients. We used the population of patients who were issued a red cell unit as the sampling frame from which to draw a random sample for inclusion in the study. The random selection of patients minimized the chances of selection bias arising as a result of convenience sampling. However, the inclusion of only one episode per patient while preventing bias arising as a result of the inclusion of some patients more than once [33] also precludes the estimation of the proportion of transfusion activity that is attributable to regularly transfused patients [2,3]. The contribution of regularly transfused patients to overall demand is likely to increase given the increasing incidence of cancer and haematological conditions such as myelodysplasia that typically require this type of supportive therapy.

The population of patients at risk of transfusion are more difficult to define and subsequently identify consistently because of variations in data recording procedures and individual hospital computer systems. In a related study, using patients who had a group-and-save sample taken, as a proxy for those patients being considered for (i.e. at risk of) transfusion, we were able to compare those at risk and transfused (as reported here) with those at risk and not transfused. As a result, the drivers of the decision to transfuse red cells could be identified and quantified by their individual relative importance when considered together. The results of this analysis will be completed in the near future and will be reported in a separate paper.

Conclusions and recommendations

The ability to track clinical usage from a population perspective, incorporating broad categories such as surgical grouping, oncology-related groups and conditions associated with bleeding, is likely to be useful to transfusion service planning their response to changes in demand driven by changes in the prevalence of these conditions over time. Change in demand is inevitable given the ageing population, increased life expectancy and broader scope of many treatment options in use and in development. However, novel approaches to the recording of transfusion episodes, such as the use of electronic medical records, are needed to improve the quality of and accuracy of information pertinent to the context of the transfusion episode.

The ability to dissect the myriad of possible clinical scenarios using a criterion-based approach is limited by the richness of the data that is usually available to populate

regression models; audit-based approaches to assessment of appropriate practice may be more productive, particularly if the use of electronic medical records that would provide a more reliable denominator, sampling frame and core dataset becomes common. In addition, a more detailed understanding of transfusion practices among clinicians is more likely to be achieved through the use of qualitative approaches.

The opportunities for a systematic approach to reduction in red cell use in those areas with a higher number of red cell units per transfusion episode are likely to be limited by the 'instability' typical of the clinical setting in which these transfusions occur. However, greater use of the single-unit transfusion followed by assessment of response may be achievable in more stable settings, either postoperatively or in oncology practice. A decade has passed since the British Committee for Standards in Haematology (BCSH) published their red cell transfusion guidelines [27]. The post-transfusion haemoglobin target (and therefore the number of units to transfuse) for any given clinical situation as well as guidance on a 'safe' transfusion threshold (when to initiate transfusion) would be useful amendments to consider in future guidelines.

References

1 Currie CJ, Patel TC, McEwan P, *et al.*: Evaluation of the future supply and demand for blood products in the United Kingdom National Health Service. *Transfus Med* 2004; **14**:19–24

2 Wells AW: Who uses blood? *Vox Sang* 2004; **87**(Suppl 2):146–148

3 Wells AW, Mounter PJ, Chapman CE, *et al.*: Where does blood go? Prospective observational study of red cell transfusion in north England *BMJ* 2002; **325**:803

4 The UK Forum. Business Information Committee Annual Report 2008/09. NHSBT 2009:1–16

5 Isbister JP: Decision making in perioperative transfusion. *Transfus Apher Sci* 2002; **27**(1):19–28

6 NHS Blood and Transplant. International comparisons of blood component usage Blood Matters 2009:10–12

7 Ballard S, Staves J, Murphy MF: Changing indications for red cell transfusion. *Transfus Med* 2007; **17**:315–316

8 Stewart A, McClelland DBL: Quality improvements on transfusion practice. The role of a national blood use reporting system. *Transfus Med* 2006; **16**:13

9 Stanworth SJ, Cockburn HA, Boralessa H, *et al.*: Which groups of patients are transfused? A study of red cell usage in London and southeast England *Vox Sang* 2002; **83**:352–357

10 Wallis JP, Wells AW, Chapman CE: Changing indications for red cell transfusion from 2000 to 2004 in the North of England. *Transfus Med* 2006; **16**:411–417

11 Wells AW, Llewelyn CA, Casbard A, *et al.*: The EASTR Study: indications for transfusion and estimates of transfusion recipient numbers in hospitals supplied by the National Blood Service. *Transfus Med* 2009; **19**:315–328

12 Biggin K, Warner P, Prescott R, *et al.*: A review of methods used in comprehensive, descriptive studies that relate red blood cell transfusion to clinical data. *Transfusion* 2010; **50**(3):711–718

13 Perkins AJ, Kroenke K, Unutzer J, *et al.*: Common comorbidity scales were similar in their ability to predict health care costs and mortality. *J Clin Epidemiol* 2004; **57**(10):1040–1048

14 Kim J, Konyalian V, Huynh R, *et al.*: Identification of predictive factors for perioperative blood transfusion in colorectal resection patients. *Int J Colorectal Dis* 2007; **22**(12):1493–1497

15 Kirkwood B, Sterne J: Essential Medical Statistics. Oxford, Wiley – Blackwell, 2003

16 Thomas D: Overview of surgical blood conservation – why bother? Proceedings of the ScotBlood Annual Conference; 2009 June 5-6; University of Sterling, Scotland

17 Anderson SA, Menis M, O'Connell K, *et al.*: Blood use by inpatient elderly population in the United States. *Transfusion* 2007; **47**:582–592

18 Northern Ireland Regional Transfusion Committee. Regional Appropriateness of Blood Transfusion Audit. 2005:1–30

19 Cobain TJ, Vamvakas EC, Wells A, *et al.*: A survey of the demographics of blood use. *Transfus Med* 2007; **17**:1–15

20 Mathoulin-Pelissier S, Salmi LR, Verret C, *et al.*: Blood transfusion in a random sample of hospitals in France. *Transfusion* 2000; **40**:1140–1146

21 Vamvakas EC, Taswell HF: Epidemiology of blood transfusion. *Transfusion* 1994; **34**:464–470

22 Bolton-Maggs PH, Murphy MF: Blood transfusion. *Arch Dis Child* 2004; **89**:4–7

23 Gillham M, Mark A: A retrospective audit of blood loss in total hip joint replacement surgery at Middlemore Hospital. *N Z Med J* 1997; **110**:294–297

24 Expert Working Group: Guidelines for red blood cell and plasma transfusion for adults and children. *CMAJ* 1997; **156**:S1–S24

25 Grey DE, Finlayson J: Red cell transfusion for iron-deficiency anaemia: a retrospective audit at a tertiary hospital. *Vox Sang* 2008; **94**:138–142

26 Nichol AD: Restrictive red blood cell transfusion strategies in critical care: does one size really fit all? *Crit Care Resusc* 2008; **10**:323–327

27 British Committee for Standards in Haematology Blood Transfusion Task Force: The clinical use of red cell transfusion. *Br J Haematol* 2001; **113**:24–31

28 Bornstein BH, Emler AC: Rationality in medical decision making: a review of the literature on doctors' decision-making biases. *J Eval Clin Pract* 2001; **7**:97–107

29 Chapman GB, Elstein AS: Cognitive processes and biases in medical decision making; in Chapman GB, Sonnenberg FA (eds): Decision Making in Health Care: Theory, Psychology and Applications. Cambridge, Cambridge University Press, 2000:183–210

30 Francis JJ, Stockton C, Eccles MP, *et al.*: Evidence-based selection of theories for designing behaviour change interventions: using methods based on theoretical construct domains to

understand clinicians' blood transfusion behaviour. *Br J Health Psychol* 2009; **14**(4):625–646

31 Francis JJ, Tinmouth A, Stanworth SJ, *et al.*: Using theories of behaviour to understand transfusion prescribing in three clinical contexts in two countries: development work for an implementation trial. *Implement Sci* 2009; **4**:70

32 Jha AK, DesRoches CM, Campbell EG, *et al.*: Use of electronic health records in U.S. hospitals. *New Engl J Med* 2009; **360**:1628–1638

33 Altman DG, Royston P: What do we mean by validating a prognostic model? *Stat Med* 2000; **19**:453–473

