

# Platelet transfusions in haematology patients: are we using them appropriately?

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## Vox Sanguinis

**Background and Objectives** A large proportion of all platelet components are given to haematology patients. As there are risks associated with their transfusion, costs associated with production, and shortages may occur, it is important that their use is appropriate.

**Study Design and Methods** The study was split into two parts, a survey to assess local practice guidelines and an assessment of platelet usage. A total of 123 hospitals completed the survey and 168 hospitals submitted data of 40 haematology patients over a 3-month period.

**Results** The organizational survey found that 36% of hospitals routinely give prophylactic platelet transfusions to patients with long-term bone-marrow failure. Also, a significant minority of hospitals administer platelet transfusions if the platelet count is below a certain threshold prior to performing a bone-marrow aspirate (11%) or a bone-marrow aspirate and trephine (23%); both of these are contrary to UK platelet transfusion guidelines. Data were collected on a total of 3402 patients, of which 3296 cases were eligible for analysis. They received approximately 46% of all platelet components issued to participating hospitals in England during the study period. The majority (69%) of platelet transfusions were prophylactic; of these only 33% were given when the platelet count was  $\leq 10 \times 10^9/L$ . Using an algorithm, based on current UK guidelines, 60% of prophylactic transfusions were appropriate, 6% could not be assessed and 34% were inappropriate. A total of 10% of all prophylactic transfusions were double the standard adult dose.

**Conclusions** There is considerable potential for decreased use of platelet transfusions with a consequent improvement in their appropriate use and cost reduction.

**Key words:** platelets, thrombocytopenia, transfusion, transfusion medicine.

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## Introduction

The largest group of patients to receive platelet transfusions are haematology patients. They have been reported to receive up to 67% of all platelet transfusions issued [1–3]. Use of platelet transfusions is increasing; data from the UK

indicate a 6% absolute increase from 2009 to 2010 [4, 5] and unpublished data from England show an increase of 8% in 2011.

National guidelines exist in many countries [6–11] and these are broadly similar to those produced by the British Committee for Standards in Haematology (BCSH) [12, 13]. These provide advice on when to transfuse platelet components to prevent bleeding (prophylactic), prior to an invasive procedure (pre-procedure), or to stop active bleeding (therapeutic).

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For prophylactic platelet transfusions, many national guidelines [6–10, 12–14] have adopted a threshold of  $10 \times 10^9/l$  if the patient has a reversible cause of bone marrow failure and does not have any additional risk factors for bleeding. This transfusion trigger is therefore an important determinant of the number of transfusions used. Strict compliance with this trigger may save costs, preserve the supply of platelets and avoid exposing patients to unnecessary risks such as bacterial infection and transfusion-related acute lung injury.

A previous study of platelet transfusions in the UK [2] showed a significant amount of platelet use outside of current guidelines. However, it was criticized for not taking potentially valid reasons for transfusion into consideration. Other observational studies of platelet transfusion use in this patient group [1, 15, 16] have also been unable to identify the proportion of patients who had valid reasons for transfusion above a threshold of  $10 \times 10^9/l$  due to insufficient available data.

This study therefore focused on the haematology patient population who is the largest user of platelet transfusions and created algorithms that took risk factors for bleeding into account as well as other valid reasons for transfusion.

## Materials and methods

All hospitals that care for haematology patients within the UK were invited to participate by means of a letter to the chief executive, medical director and clinical audit manager. Copies of this letter were sent by e-mail to hospital blood transfusion laboratory managers, transfusion practitioners and haematologists with responsibility for blood transfusion. Non-responders were sent reminder letters and were contacted by telephone to encourage recruitment. Eligible hospitals were identified via the regional transfusion committees.

The study was split into two parts, an organizational survey to assess local guidelines and a clinical study to assess current transfusion practice.

### Data collection

An organizational, paper-based survey (Appendix S1) was sent to the consultant haematologist with responsibility for blood transfusion at each participating hospital. This survey addressed the availability of local guidelines for platelet transfusion, and if present, requested information on their specific recommendations.

In addition, hospitals were asked to collect data on up to 40 separate haematology patients receiving a platelet transfusion over a 3-month period (September to December 2010). If fewer than 40 individual patients were transfused

during the 3-month study period, then all patients transfused were included. All haematology patients regardless of age or gender were eligible for inclusion. Hospitals had the choice of collecting data on a prospective or retrospective basis, depending on their operational preferences, provided that the cases were consecutive to avoid selection bias. Detailed information was collected on the initial platelet transfusion including: reason for platelet transfusion; type of procedure performed; severity of bleeding prior to transfusion; pre-transfusion platelet count; risk factors for bleeding; post-transfusion platelet count; whether the platelet component was due to expire at midnight; whether the patient had any significant bleeding in the 24 h following the platelet transfusion and whether the patient had a transfusion reaction. The total number of platelet transfusions for each patient, during the study period, was also collected.

Data on the type of platelet product, ABO compatibility, irradiation and HLA alloimmunization status of the recipient were not collected. All platelet transfusions in the UK are leucocyte-depleted, and over 80% are collected via apheresis. Platelet transfusions are routinely ABO and Rh identical.

Data on who requested the platelet transfusion were not recorded. This study was designed to assess standards of care and collected fully anonymized routinely available data. No hospital received remuneration for participation in this study. This study did not require formal ethical review according to guidance from the National Research Ethics Service [17].

### Algorithms

Three separate algorithms (prophylactic, pre-procedure and therapeutic) were designed a priori to evaluate whether a transfusion was appropriate (Appendices S2–S4). These were applied to the data centrally after data collection. These took into consideration the recommendations in BCSH guidelines [12–14, 18–21], the platelet count and timing, diagnosis and whether an individualized platelet count threshold or additional risk factors for bleeding (e.g. infection, fever, bleeding diathesis) were documented in the notes. In addition, two pragmatic reasons for transfusion were deemed appropriate. First, if the patient was an outpatient or due to be discharged that day and their platelet count was  $\leq 20 \times 10^9/l$  and expected to fall to  $< 10 \times 10^9/l$  before their next clinic evaluation. Secondly, if the patient was an inpatient who had a platelet count  $\leq 20 \times 10^9/l$  and it was expected to fall to  $< 10 \times 10^9/l$  within 24 h (i.e. they would receive an ‘appropriate’ transfusion the following day), and the platelet components were due to expire at midnight and would be otherwise wasted.

## Data analysis

The overall analysis of the data is descriptive, with results presented as percentages for categorical data and as medians and interquartile ranges (IQR) for numerical data. Any missing data are reflected by variations in the denominators. A total of 95% confidence intervals were computed for the estimates of appropriateness of transfusion. The  $\chi^2$  test was used to compare between inpatients and outpatients receiving prophylactic transfusions in regard to these transfusions being outside of guidelines and in regard to patients receiving a double-dose transfusion.

## Results

A total of 152/167 (91%) of eligible hospitals in England & North Wales participated. Hospitals in Wales (7), Northern Ireland (1) and Scotland (12) also participated. In all, 123/172 (72%) of hospitals participated in the organizational survey and 168/172 (98%) provided clinical data.

### Organizational survey

In all, 96% (118/123) of the hospitals who returned the survey had written guidelines for platelet transfusions, and in 83% (102/123) the same common guidelines were used for adults and children. For the remainder of the survey results, if hospitals had separate guidelines for adults and children (18 hospitals), the results of the survey for the adult guidelines are reported. A total of 98% (120/123) guidelines used a threshold of  $10 \times 10^9/l$  for prophylactic platelet transfusions in stable patients with a reversible cause of bone marrow failure. 59% (73/123) of hospitals treated haematology patients with intensive, complex chemotherapy regimens (BCSH criteria levels 2b or 3) [22] which would be expected to result in frequent and severe thrombocytopenia.

The majority of hospitals increased this prophylactic threshold for situations considered to increase the risk of bleeding. For example, 79% (97/123) of hospitals increased their threshold if a patient has an infection, and 68% (84/123) increased this to  $20 \times 10^9/l$ . However, there was some variation in other risk factors considered significant enough to increase the transfusion threshold and the revised platelet count used. For example, only 28% (33/120; three hospitals did not answer the question) increased their threshold if the patient was receiving therapeutic antifungal medication. Also, in patients with disseminated intravascular coagulation, 35% (43/123) used a threshold of  $20 \times 10^9/l$  and 25% (31/123) used a threshold of  $50 \times 10^9/l$ .

Although national guidelines [13] do not recommend routine prophylactic platelet transfusions for stable patients

with long-term bone marrow failure, 36% (44/123) of hospitals indicated that these would be given at a count of either  $<10 \times 10^9/l$  or  $<20 \times 10^9/l$ .

Most hospitals used the national guidelines to guide practice prior to invasive procedures with a usual threshold of  $50 \times 10^9/l$  (50–85%) (62/123 for surgery excluding the eye and brain to 105/123 for indwelling line insertion), or  $100 \times 10^9/l$  (85%; 105/123) for procedures involving the eyes or brain. An exception to this was for epidural anaesthesia where a more commonly stated threshold was  $80 \times 10^9/l$  (42%; 52/123) compared to the BCSH threshold of  $50 \times 10^9/l$  (37%; 45/123).

Despite national guidelines [8, 13] to the contrary, a significant minority of hospitals indicated that a platelet transfusion would be required if the platelet count was below a certain threshold prior to performing a bone marrow aspirate (11%, 14/123) or a bone marrow aspirate and trephine (23%, 28/123).

The recommended threshold [12] of  $20\text{--}40 \times 10^9/l$  prior to line insertion or lumbar puncture in children has not been widely adopted and was not used in any of the paediatric hospitals.

A total of 58% (71/123) of hospitals indicated that requests were discussed with a haematologist (trained or a supervised trainee).

## Clinical data

### Sample characteristics

In all, 168 hospitals submitted clinical data on 3402 patients (Fig. 1), 18 cases were excluded due to lack of data and 88 cases were excluded because they were not haematology patients. The remaining 3296 cases were analysed. There was a median of 18 patients (IQR 9–30) enrolled per hospital. These cases accounted for an estimated 46% of all platelet components issued to participating hospitals during the study period.

A total of 68% (2225/3296) of all cases were inpatients and 32% (1071/3296) were outpatients. The median age was 64 years (IQR 49–74 years). A total of 60% (1971/3296) of included cases were aged 60 years or over and 7% (229/3296) were under 18 years of age. The most common underlying haematological diagnoses were acute myeloid leukaemia (962/3296; 29%), lymphoma (617/3296; 19%) and myelodysplasia (364/3296; 11%) (Table 1). Two-thirds (2283/3296, 69%) of the platelet transfusions was prophylactic.

### Pre-transfusion platelet count

A pre-transfusion platelet count was performed less frequently in outpatients than inpatients. It was carried out within 24 h in 96% (2130/2225) of inpatients and within 48 h in 86% (916/1071) of outpatients.

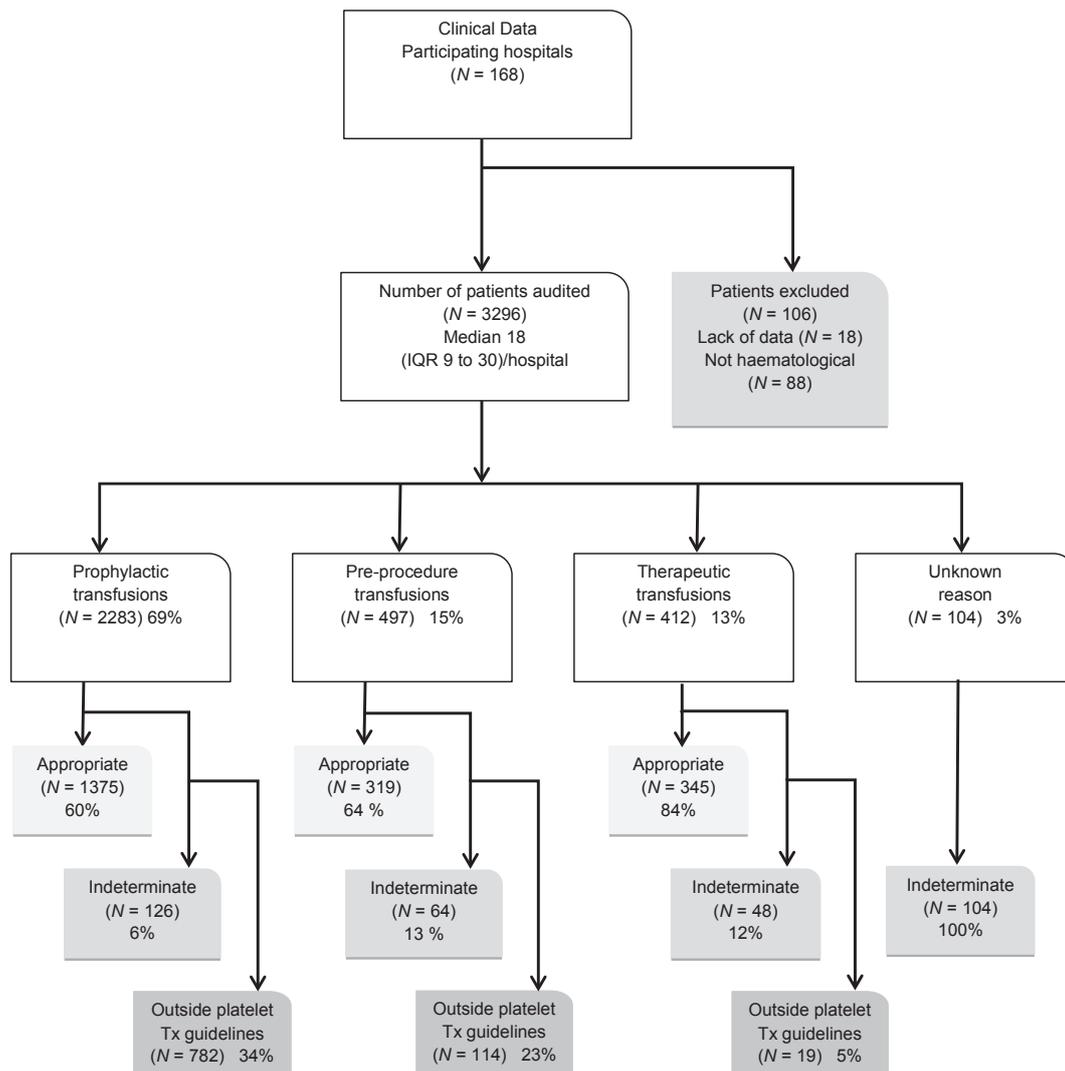


Fig. 1 Flow diagram of cases included in study.

### Prophylactic platelet transfusions

A total of 69% (2283/3296) of all the transfusions were prophylactic (Table 2). Only 34% (715/2132) of adult cases and 23% (34/151) of paediatric cases who had a reversible cause of bone marrow failure received these when their platelet count was  $\leq 10 \times 10^9/l$ . Overall, the median pre-transfusion platelet count was  $12 \times 10^9/l$  (IQR 8–18). The median platelet count increment was  $17 \times 10^9/l$  (IQR 7–31).

Using the algorithm to further evaluate the appropriateness of transfusion, 60% (1375/2283) were deemed appropriate, 95% confidence interval ranged from 58.2 to 62.2% (Table 2). The main reasons for a platelet transfusion to be classified as appropriate when the platelet count was  $>10 \times 10^9/l$  were: an individualized threshold documented in the notes, infection or the platelet count was expected to fall before the next evaluation.

A total of 34% (782/2283) of prophylactic transfusions were considered to be inappropriate (Table 2). These were mostly because of transfusion above the recommended platelet count threshold but also 8% (189/2283) were administered as prophylactic transfusions to patients with myelodysplastic syndrome (MDS) who did not have additional risk factors for bleeding. In all, 2% (49/2283) were given to patients with immune thrombocytopenic purpura (ITP) or thrombotic thrombocytopenic purpura (TTP). An additional 6% (126/2283) were considered to be indeterminate (possibly inappropriate) because no recent platelet count had been performed.

A higher proportion (41%, 353/851) of outpatient platelet transfusions were outside guidelines than inpatient patient transfusions (30%, 429/1432),  $P < 0.001$ ,  $\chi^2$  test.

**Table 1** Haematological diagnosis of patients in study ( $N = 3296$ )

	Number	Percentage
Acute myeloid leukaemia	962	29
Lymphoma	617	19
Myelodysplasia and myelodysplastic/myeloproliferative neoplasms	438	13
Myeloma/plasma cell dyscrasia	296	9
Acute lymphocytic leukaemia	211	6
Other <sup>a</sup>	179	5
Aplastic anaemia	173	5
Chronic lymphocytic leukaemia and other chronic leukaemias	152	5
Myeloproliferative disorders (including myelofibrosis and chronic myeloid leukaemia)	116	4
Immune thrombocytopenia	105	3
Other acute leukaemia	37	1
Thrombotic thrombocytopenic purpura	10	<1
Total	3296	100

<sup>a</sup>Includes haemoglobinopathies, familial thrombocytopenia, platelet function disorders, Fanconi's anaemia, haemophagocytic lymphohistiocytosis and other rare haematological disorders.

A total of 10% (220/2277) of prophylactic transfusions were double-dose transfusions [defined as two adult doses (apheresis or buffy coat) given in one transfusion episode]. In 6 cases the dose was not reported. The majority, 73% (160/220) of double-dose transfusions, were administered to inpatients, and inpatients were more likely to receive a double-dose transfusion than outpatients (11% (160/1432) vs. 7% (60/851) respectively,  $P = 0.002$ ). A total of 36% (80/220) of these double-dose transfusions were considered to be inappropriate according to the algorithm (i.e. the patient should not have received a single (standard) dose platelet transfusion) and a further 5% (10/220) were indeterminate (see previous definition).

Only 1% (23/2283) of patients had significant bleeding in the 24 h following the prophylactic platelet transfusion. In all, 15 of these cases required extra blood product support and four of these cases had bleeding that caused hemodynamic compromise (defined as a drop in systolic or diastolic of >30 mmHg).

### Pre-procedure platelet transfusions

A total of 497 patients had 536 procedures (Tables 3 and 4). The most common procedure was line insertion (28%), followed by surgery not involving the eye or brain (23%). In 12% of procedures, a bone-marrow aspirate and/or trephine was performed, and in 9% (45/497) of patients this was the only procedure performed.

In 81% (402/497) of patients, the transfusion was given within the 6 h period preceding the procedure. However,

**Table 2** Prophylactic platelet transfusions ( $N = 2283$ )

	Number	Percentage
Appropriate	1375	60
Reversible cause of bone marrow failure; platelet count $<10 \times 10^9/l$ ; recent blood count; not ITP or TTP	698	31
Individualized threshold in notes	184	8
Infection	174	8
Platelet count expected to fall to $<10 \times 10^9/l$ before next evaluation <sup>a</sup>	136	6
Bleeding diathesis/increased bleeding risk	56	2
Other <sup>b</sup>	55	2
Platelet components expire at midnight and platelet count $\leq 20 \times 10^9/l^c$	53	2
Severe mucositis	10	<1
Severe leucocytosis	5	<1
Treatment with ATG/Bortezomib	4	<1
Indeterminate	126	6
Platelet count not performed	29	1
Platelet count too old	72	4
Unknown	25	1
Outside platelet transfusion guidelines	782	34
No reason given for transfusion above threshold of $10 \times 10^9/l^d$	361	16
MDS with no additional risk factors for bleeding	189	8
Transfusion above guideline recommendations for reasons given <sup>d</sup>	183	8
ITP	43	2
TTP	6	<1
All	2283	100

ITP, immune thrombocytopenic purpura; MDS, myelodysplastic syndrome; TTP, thrombotic thrombocytopenic purpura.

<sup>a</sup>To allow for pragmatic management of outpatients.

<sup>b</sup>Includes factors such as minor bleeding, minor infection, liver dysfunction, hazardous job.

<sup>c</sup>To avoid wastage of platelet components in inpatients who are expected to have a platelet count  $<10 \times 10^9/l$  within 24 h.

<sup>d</sup>Excludes patients with ITP/TTP or MDS.

only 30% (151/497) of cases had a post-transfusion platelet count taken prior to the procedure to assess response, although this is recommended [13]. In the majority of cases (79%; 274/346), there was no obvious reason for this omission.

Using the algorithm to further evaluate the appropriateness of transfusion 64% (319/497) were considered to be appropriate, 95% confidence interval ranged from 59.8 to 68.4% (Table 4). The major reasons for inappropriateness were transfusions before bone marrow procedures in 9% (45/497) (it is explicitly stated in the national guidelines that this usage is unnecessary) [13] and transfusion above recommended thresholds in 14% (69/497).

**Table 3** Type of procedure performed ( $N = 536$  procedures in 497 patients)

	Number	Percentage
Indwelling line insertion	152	28
Surgical procedure not involving eye or brain	122	23
Other <sup>a</sup>	75	14
Bone marrow aspirate and/or trephine	67	12
Lumbar puncture	51	10
Endoscopy only	23	4
Organ biopsy	21	4
Endoscopy and biopsy	12	2
Surgery/biopsy on eye/brain	6	1
Epidural anaesthetic	4	<1
Unknown	3	<1
Total	536	100

<sup>a</sup>Included: line removal (35), aspiration (11), drain insertion (8), interventional radiology (6), apheresis (5), skin biopsy (3), vaginal delivery (3), catheter insertion (2), injection (1).

**Table 4** Pre-procedure platelet transfusions ( $N = 497$ )

	Number	Percentage
Appropriate	319	64
Indeterminate	64	13
Platelet count not performed/too old	46	9
Endoscopy without biopsy	18	4
Outside platelet transfusion guidelines	114	23
Bone marrow aspirate and/or trephine alone	45	9
Transfusion above guideline recommendations	69	14
All	497	100

If strict application of national guidelines [12] and a threshold of  $40 \times 10^9/l$  had been applied to all paediatric cases who had either a lumbar puncture or central line inserted, fewer than 1% (4/497) of transfusions would have been re-categorized as outside platelet transfusion guidelines.

A total of 5% (23/497) of patients had excessive bleeding in the 24 h following the procedure. In 20 cases, extra blood products were required (12/20 RBC transfusion, 14/20 platelet transfusion, 2/20 FFP, 1/20 cryoprecipitate) and in four cases this caused hemodynamic compromise. Eight cases needed other interventions to stop the bleeding (3/8 anti-fibrinolytics, 3/8 surgery, 4/8 cautery or pressure was applied).

### Therapeutic platelet transfusions

The most common types of bleeding were epistaxes, melaena and large/multiple bruises (Tables 5 and 6).

Using the algorithm to assess the appropriateness of transfusion (including the diagnosis and severity of

**Table 5** Types of haemorrhage WHO grade 2 or above ( $N = 467$  haemorrhages in 371 patients)

Type	Number	Percentage
Gastrointestinal bleeding (101 episodes)		
Haematemesis	30	6
Visible blood in stool	33	7
Melaena	52	11
Skin (85 episodes)		
Petechiae (spreading/confluent)	33	7
Bruises (large or multiple)	45	10
Nosebleed lasting $\geq 30$ min	65	14
Genito-urinary bleeding (55 episodes)		
Visible haematuria	33	7
Abnormal vaginal bleeding	22	5
Bleeding from mouth or throat (50 episodes)		
Symptomatic blood blisters	31	7
Lasting $\geq 30$ min	23	5
Abnormal bleeding at site of previous procedure	27	6
Unknown	27	6
Haemoptysis	20	4
Central nervous system (18 episodes)		
Intracranial haemorrhage with neurological signs	15	3
Intracranial haemorrhage without neurological signs	3	<1
Eye (eight episodes)		
Retinal haemorrhage with visual impairment	3	<1
Retinal haemorrhage without visual impairment	5	1
All	467	100

bleeding), 84% (345/412) were appropriate and 95% confidence interval ranged from 79.8 to 87.2% (Table 6). In 18% (73/412) of cases, the bleeding caused haemodynamic compromise (defined previously) and in 21% (87/412) additional blood products were required. Within the audit there were 18 cases of intracranial haemorrhage (ICH) (15/18 with neurological signs) and 8 cases of retinal haemorrhage (3/8 with visual impairment). Only 6% (1/18) of ICH cases had a pre-transfusion platelet count  $<10 \times 10^9/l$  and 44% (8/18) had a platelet count  $<20 \times 10^9/l$ . None of the cases of retinal haemorrhage with visual impairment had a platelet count  $<10 \times 10^9/l$ , and two had a pre-transfusion platelet count  $<20 \times 10^9/l$ . It was unknown whether any of these patients had pre-existing pathology that could have predisposed them to bleeding.

**Table 6** Therapeutic platelet transfusions ( $N = 412$ )

	Number	Percentage
Appropriate	345	84 <sup>b</sup>
WHO grade 2	220	53
WHO grade 3	38	9
WHO grade 4	87	21
Indeterminate	48	12
WHO grade I bleeding <sup>a</sup>	38	9
Insufficient information to grade bleeding <sup>a</sup>	10	3
Outside platelet transfusion guidelines	19	5
ITP (not life-threatening bleeding)	19	5
TTP (not life-threatening bleeding)	0	0
All	412	101 <sup>b</sup>

ITP, immune thrombocytopenic purpura; TTP, thrombotic thrombocytopenic purpura.

<sup>a</sup>Excluding ITP/TTP.

<sup>b</sup>Due to rounding.

In 58% (239/412) of cases bleeding stopped following the platelet transfusion but in 39% (159/412) bleeding continued. In those that continued to bleed, 70% (112/159) required extra blood product support and 43% (68/159) required other interventions.

#### *Reason for platelet transfusion unknown*

In 3% (104/3296) of cases, the auditor was unable to determine the reason why the platelet transfusion was given.

#### *Further platelet transfusions during the audit period*

A total of 76% of patients (2517/3296) had further platelet transfusions during the study period, 23% (770/3296) did not and in 9 this information was not reported. Information regarding other platelet transfusions was provided for 3259 cases. For these cases, the median number of transfusions was 5 (IQR 3–11).

To obtain an understanding of the percentage of platelet units used by the cases in the study, the Blood Stocks Management Scheme provided platelet issue data for the 3-month period for participating sites (36 331 units). A conservative estimate of the number of platelet components used by these cases was calculated by adding the number of units used in the initial transfusion episode to the number of additional transfusion episodes during the study period. This gave a total of 16 703 units which represents 46% (16 703/36 331) of all units issued to these sites over the study period.

#### *Complications of platelet transfusions*

A total of 4% (120/3296) of all cases suffered an adverse event within 24 h of the platelet transfusion. In 35% (42/120) this was considered to be a transfusion reaction. No deaths were reported, two cases had a severe allergic

reaction, one case developed hypotension, six cases had fever with additional problems and the remaining 33 had mild reactions of either fever only (3) or allergy (30). In 51% (61/120) of cases the adverse event was not considered transfusion-related, and 14 of these cases died within 24 h. In 14% (17/120), it was unknown whether or not the adverse event was transfusion-related.

## Discussion

### Key findings

Virtually all hospitals endorse a platelet transfusion threshold of  $10 \times 10^9/l$  in stable patients with reversible bone marrow failure and no additional risk factors for bleeding (as recommended by UK national guidelines [13]). This shows much greater consistency than a previous survey [23], which pre-dated the current national guidelines. However, there is still great variability in the use of platelet transfusions in patients with additional risk factors for bleeding. Variability in these local practices may be partially explained by the lack of evidence base to support some of the recommendations in national guidelines.

A total of 28% (915/3296) of all transfusions could have been avoided if practice complied with national guidelines. The main reasons that prophylactic platelet transfusions were classified as outside of guidelines were: transfusion above a defined threshold platelet count; transfusion to patients with MDS. In addition, 2% (49/2283) of prophylactic platelet transfusions were given to patients with ITP or TTP. The main reasons that pre-procedure platelet transfusions were outside guidelines were: the only procedure performed was a bone marrow aspirate and/or trephine; transfusion above the guidelines without an individualized threshold specified in the notes. If a patient requires a higher transfusion threshold than the guidelines recommend because of valid reasons indicating an increased bleeding risk, this should be clearly documented in the patient's notes. Without it, communication between haematologists, surgeons, radiologists and anaesthetists may be inadequate and could harm the patient by increasing their risk of severe bleeding if the platelet count is not raised to the appropriate level. Only one of the other international guidelines [6–11] reviewed specifically mentioned bone marrow biopsy [8] and stated it was safe for this to be performed when platelet counts  $<20 \times 10^9/l$ .

In all, 10% (220/2283) of prophylactic platelet transfusions were double-dose platelet transfusions. A recent large randomized controlled trial has shown no difference in the number of patients who had significant bleeding (WHO grade 2 or above) when they received low ( $1.1 \times 10^{11}/m^2$ ), intermediate ( $2.2 \times 10^{11}/m^2$ ) or high dose platelet transfusions ( $4.4 \times 10^{11}/m^2$ ) [24]. In the UK, a single adult

therapeutic dose platelet transfusion ( $2.4 \times 10^{11}$  platelets) is close to the low-dose platelet transfusion arm of this study. The dose of platelet components used in the UK has to comply with a national standard that at least 75% of components contain  $2.4 \times 10^{11}$  platelets per adult dose [25]. A pragmatic reason why double-dose platelet transfusions may be used is to increase the transfusion interval in patients requiring regular outpatient transfusions. However, in this audit, the majority of double-dose transfusions were given to inpatients and a higher proportion of double-dose platelet transfusions were given to inpatients compared to outpatients (11% vs. 7%).

### Study in context

Since the last UK national guidelines were published in 2003 [13], there have been several disease-specific and procedure-specific national guidelines that have added more recommendations regarding when platelets should be given [14, 18, 19, 21]. In addition, further evidence from systematic reviews [26] and clinical studies [27, 28] has been published. Recommendations from these more recent guidelines, reviews and studies sometimes contradict the 2003 guideline making it difficult to determine which should be followed. For example, the 2003 guidelines [13] recommend a threshold of  $50 \times 10^9/l$  prior to an epidural anaesthetic, whereas a recent systematic review [26] recommends a threshold of  $75\text{--}80 \times 10^9/l$ . The 2003 guidelines [13] also recommend a threshold of  $50 \times 10^9/l$  prior to insertion of an indwelling central venous catheter, whereas two recent studies recommend a safe threshold of  $20\text{--}25 \times 10^9/l$  [27, 28].

Platelet transfusions are given to prevent and treat bleeding. The type and incidence of bleeding cannot be easily compared to platelet transfusion studies. This study only looked at one platelet transfusion episode in detail whereas the most recent trials [23, 29] looked at the overall incidence of bleeding for patients during the whole period of thrombocytopenia. Of note, in this study, 50% (13/26) of episodes of ICH and retinal haemorrhage occurred at pre-transfusion platelet counts above  $20 \times 10^9/l$ . This is consistent with a large retrospective study that found no correlation between the platelet count and moderate and severe bleeding [30].

In this study the incidence of transfusion reactions was 1% (42/3296), and only 0.1% (3/3296) was clearly moderate or severe in nature. However, any adverse reaction may have: increased morbidity, in already sick patients; precipitated investigations and, in some, led to a delayed discharge from hospital. While this is an acceptable risk and use of resources in patients when the transfusion is appropriate, it is insupportable for the 28% of transfusions considered unnecessary.

Patient management should balance the benefits of treatment against its inherent risks in the way that is most acceptable to the patient. In the field of haematology this often involves the use of aggressive chemotherapy regimens in the pursuit of cure. Supportive therapy, to prevent the side-effects of treatment, requires the use of antibiotics, anti-emetics and blood products without which these intensive regimens would not be possible. Platelet transfusions are only one component of a myriad of supportive measures. This situation has two main consequences. First, the risks of platelet transfusion may be forgotten when compared to those of the primary treatment. In this study only 3/3296 patients suffered a moderate/severe transfusion reaction within 24 h of the transfusion while 14 of these patients died from other causes during the same time period. Secondly, the task of implementing this therapy is often left to the more junior members of the team. They frequently have little experience of looking after patients with such low platelet counts but know that it is their responsibility to prevent the patient from bleeding. Under these circumstances, it should come as no surprise that, in this study, only 60% of prophylactic, 64% of pre-procedure and 84% of therapeutic transfusions were considered appropriate (using algorithms based on national guidelines) and, in addition, 10% of all prophylactic transfusions were double-dose transfusions.

### Limitations of the study

Any conclusions from this report should acknowledge study limitations. Data collected were limited to the information documented in patient records. There was no method of verification of source data from consecutive patients or data entry quality control. However, the study used a web-based data collection tool that led to few incomplete data fields. Only 18 cases were excluded due to a lack of data. The large sample size should also provide a greater degree of confidence in the main findings, although this does not prevent systematic bias within the study.

### Conclusions

This was a large study and covered a significant percentage of all platelet use. It is therefore well placed to identify areas where practice could be improved. As the majority of transfusions were to patients 60 years or over and the age of the population is increasing, platelet use is likely to increase if no change to current practice occurs. The results clearly show that platelet transfusion practice could be improved by adherence to guidelines and in many cases this would improve appropriateness and reduce use with

consequent improvements in patient safety and a reduction in cost.

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## Conflict of interest

The authors declare that they have no conflicts of interest relevant to the manuscript submitted to *Vox Sanguinis*.

## Author contributions

Lise Estcourt and Janet Birchall: clinical lead for the study and contributed to the design and conduct of the study and the final report. Derek Lowe is a statistical expert and contributed to the design of the study and final report. John Grant-Casey is an audit expert and contributed to the design and conduct of the study and final report. Megan Rowley and Michael Murphy: content expert and contributed to the design of the study and final report.

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## Supporting information

Appendix S1 Survey of local guidelines.

Appendix S2 Study algorithm for prophylactic platelet transfusions.

Appendix S3 Study algorithm for pre-procedure platelet transfusions.

Appendix S4 Study algorithm for therapeutic platelet transfusions.

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