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National Comparative Audit of Blood Transfusion

NHS Blood and Transplant

2010 Re-audit of the Use of Platelets in Haematology

April 2011

St. Elsewhere's NHS Foundation Trust

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ABBREVIATIONS

ATG	Anti-Thymocyte Globulin
BCSH	British Committee for Standards in Haematology
BSMS	Blood Stocks Management Scheme
CQC	Care Quality Commission
DIC	Disseminated Intravascular Coagulation
HSC	Health Service Circular
IQR	Interquartile range
ITP	Immune thrombocytopenia
MDS	Myelodysplasia
NBTC	National Blood Transfusion Committee
NCABT	National Comparative Audit of Blood Transfusion
NHSBT	NHS Blood and Transplant
TTP	Thrombotic Thrombocytopenic Purpura
vCJD	variant Creutzfeld Jacob Disease
WHO	World Health Organisation

EXECUTIVE SUMMARY & RECOMMENDATIONS

INTRODUCTION

A large percentage of platelets (27 to 57%) is given to haematology patients [1] [Appendix 2] and use is largely prophylactic to prevent haemorrhage [2]. As there are costs associated with production, risks associated with transfusion and shortages may occur, it is important that use is appropriate.

METHODS

139/153 eligible NHS trusts in England and N. Wales participated. Sites in Wales (7), N. Ireland (1), and Scotland (12) as well as 2 independent hospitals also participated.

The audit was split into two parts, an organisational audit to assess local guidelines and a transfusion episode audit to assess practice. Sites[1] were asked to collect data on up to 40 haematology patients receiving a platelet transfusion over a 3 month period (September to December 2010).

RESULTS

ORGANISATIONAL AUDIT

123 sites (trusts or hospitals) submitted organisational data.

96% (118/123) of sites had written guidelines for platelet transfusions, and in 88% these were accessible on the hospital intranet.

Audit of platelet use was stated to occur in 50% (61/123) of sites, however in only 43% (26/61) of these had this occurred within the last 12 months.

82% (101/123) of sites had the same guidelines for adult and paediatric patients. There were 4 paediatric hospitals. No unique or common changes were apparent when paediatric guidelines were compared to adult or combined adult and paediatric guidelines therefore the data on the 119 adult or combined adult and paediatric guidelines were considered representative.

In patients with reversible bone marrow failure 98% (117/119) of sites use a platelet count threshold of 10×10^9/L for prophylactic transfusion. The majority increase this threshold for situations considered to increase the risk of bleeding however there was variation in the revised platelet count used.

[1] Data were submitted by trusts, as a whole, or by individual hospitals. Therefore the generic term "sites" will be used throughout this report to refer to both.

36% (43/119) of sites give patients with long term bone marrow failure routine prophylactic platelet transfusions.

Prior to performing a bone marrow aspirate or a bone marrow aspirate and trephine 12% and 23% of sites respectively use routine platelet transfusion below a specified count.

In 64% of all sites blue light delivery time was greater than one hour.

CLINICAL PRACTICE

3296 transfusion episodes were analysed.

60% of patients were aged 60 years or over and 7% of patients were under 18 years of age.

The most common haematological diagnoses were acute myeloid leukaemia (29%), lymphoma (18%) and myelodysplasia (11%).

There was 92% (3046/3296) compliance with the requirement for a recent pre-transfusion platelet count.

The reason for the transfusion was only clearly documented in the notes in 72% of cases. However, auditors were able to identify the reason for transfusion as prophylactic in 69% (2283/3296), pre-procedure in 15% (497/3296), therapeutic in 13% (412/3296) and unclear in 3% (104/3296).

Using a conservative estimate - 46% of total platelets issued to participating sites over the audited period were used by the audited cases.

In 23% of cases (764/3296) at least one unit was due to expire at midnight on the day of transfusion.

1% (42/3296) of all cases were considered to have had a reaction to the platelet transfusion.

Prophylactic platelet transfusions

Adult: - 2132 cases. 34% were given when the pre-transfusion platelet count was $\leq$ 10 x 10^9/L.

Paediatric: - 151 cases. 23% were given when the pre-transfusion platelet count was $\leq$ 10 x 10^9/L. A further 18% were clearly compliant with BCSH guidelines, which specifies alternative thresholds for specific risk factors in paediatric patients.

Using an algorithm (See Appendix 1) developed for this audit 60% were appropriate.

Pre-procedure platelet transfusions

In 9% of cases the only procedure performed was a bone marrow aspirate and/or trephine biopsy.

In 81% of patients the transfusion was given within 6 hours of the procedure.

Only 30% of cases had a post transfusion platelet count checked prior to the procedure.

Using an algorithm developed for this audit 64% were appropriate.

The most common reason for a transfusion to be classified as outside of guidelines, in this category, was when the only procedure performed was a bone marrow aspirate and/or trephine biopsy.

Therapeutic platelet transfusions

The most common types of bleeding were nose bleeds, malaena and large or multiple bruises.

Using an algorithm developed for this audit 84% (345/412) were considered appropriate. The only patients classified as outside of guidelines were ITP/TTP with non-life-threatening bleeding.

RECOMMENDATIONS

1. The BCSH guidelines on the use of platelet transfusions[3] should be updated.

2. Until revised guidelines are available, local guidelines should be based on current BCSH guidelines and, in particular, should specify that a platelet transfusion is **not** required routinely: –

   - Prior to bone marrow aspiration and biopsy
   - As prophylaxis in stable patients with long term bone marrow failure.

3. The reason for transfusion should be clearly documented in the notes/patient's record including any individual threshold platelet count agreed for that patient.

4. A platelet count is required within a few hours prior to prophylactic platelet transfusion. As a minimum this should be within 24 hours in in-patients and within 48 hours in out-patients.

5. If platelets are necessary pre-procedure they should be transfused close to the procedure to obtain maximum benefit but allow time for a post transfusion platelet count to be taken to assess response. A platelet count taken 10 minutes after a platelet transfusion has been shown to be equivalent to the 1 hour platelet count increment [4].

6. Information technology solutions will make data to audit transfusion practice readily available. The BSMS/NHSBT are working to progress this objective.

INTRODUCTION

WHY WAS THIS AUDIT NECESSARY?

In the year 2007 – 2008, over 250,000 platelet concentrates were issued to hospitals within the UK. A large percentage of these (27 to 57%) are given to haematology patients [1] [Appendix 5] and use is largely prophylactic to prevent haemorrhage [2]. As there are costs associated with production, risks associated with transfusion and shortages may occur it is essential that use is appropriate.

The previous national comparative audit showed a significant deviation of practice from national guidelines [2]. However, the results were criticised for not taking into account adequately factors which may alter the transfusion threshold for each patient.

This audit will therefore use standards to assess the use of platelets in accordance with national guidelines and recommendations from the previous audit. In addition it will assess appropriateness using algorithms which take into account supplementary requested information.

WHAT DID THIS AUDIT AIM TO ACHIEVE?

- To survey compliance with the previous audit's recommendations:
  - local written guidelines for the transfusion of platelets in haematology patients
  - regular local audit to assess compliance against the guidelines
- To survey whether local guidelines are compliant with national published guidelines where there are specific recommendations.
- To audit platelet transfusion management of haematological patients with respect to the use of platelet transfusions.
- To assess the extent of variation in practice with respect to each of the above.
- Following the publication of the audit findings, to work with participating hospitals to achieve a reduction in the variability of platelet transfusion practice.

WHO ARE THE PRINCIPAL STAKEHOLDERS?

- NHS hospitals
- Independent hospitals
- NHS Blood and Transplant (NHSBT)
- National Blood Transfusion Committee (NBTC)

DATA TRANSPARENCY AND DATA SHARING

In line with current practice within national clinical audits, the National Comparative Audit of Blood Transfusion (NCABT) is exploring ways of making key results available to organisations such as the Care Quality Commission (CQC).

At present we supply to the CQC the names of those hospitals and NHS Trusts who contribute data to our audits.

In addition, we intend to share the following information with the CQC.

Data item – key performance indicator	Reason for sharing
Locally written guidelines were available	Key to safe management of patients is to have local consistent guidelines. The only way to achieve this is in a written format.
Reason for platelet transfusion was documented in the notes	Requirement of HSC 2007/01

All participants have given permission for their information to be included at the time of agreement to participate in the audit.

METHODS

HOW WERE NHS TRUSTS AND INDEPENDENT HOSPITALS RECRUITED?

All NHS Trusts and independent hospitals in England were invited to participate in the audit provided they transfuse platelets to haematology patients. Trusts and hospitals in Wales, Northern Ireland and Scotland were also invited to participate.

Hospitals were intended to be the unit of involvement, since practice may vary from hospital to hospital within a Trust. Trusts were asked to nominate their participant hospitals. However, data were submitted by Trusts as a whole and by individual hospitals. Therefore, the term "sites" is used throughout this report to refer to either Trust or hospital.

A letter, explaining the purpose of the audit, the proposed timescale, and the proposed dataset to be collected, was sent to the Medical Director in each English NHS Trust. Electronic copies of this letter were sent via email to Chairs of HTCs, Trust Transfusion Laboratory Managers, Transfusion Practitioners, and Consultant Haematologists with responsibility for blood transfusion. For independent hospitals a letter was sent to the hospital manager.

SAMPLING STRATEGY

Sites were asked to collect data over a three month period. The target sample was 40 haematology patients receiving a platelet transfusion over a 3 month period, or if less than 40 transfusions were performed then all patients within a 3 month period (September to December 2010). All patients, regardless of age or gender, were eligible for inclusion in the sample but they could only be entered once within the audit period. Information on the initial platelet transfusion was collected in detail, and the total number of platelet transfusions for each patient, during this time period, was also collected to allow determination of the proportion of platelet transfusions audited. Participants had the choice of collecting data on a prospective or recent retrospective basis, depending on their operational preferences.

STANDARDS

See next section.

DATA COLLECTION METHOD

The organisational audit was a paper based audit tool to assess local guidelines on platelet transfusions. The organisational audit form was sent to the Consultant Haematologist with responsibility for transfusion within that hospital. Clinical data for this audit was collected by a Transfusion Practitioner or a similarly qualified person. Data entry for the clinical audit was directly onto the audit tool webpage designed for the purpose.

PILOT

12 hospitals agreed to pilot the audit and during July 2010 completed the organisational audit tool once and tested the patient audit tool on 10 patients.

ANALYSIS AND PRESENTATION OF RESULTS

Data from the organisational questionnaire and clinical audit were analysed using SPSS version 19

National results are presented in this report as percentages for categorical data and as medians and interquartile ranges (IQR) for numerical data.

To facilitate benchmarking individual site results are shown alongside the national results. Some of the 'Your site' results are based on small numbers of patients; sites need to take account of this when interpreting their own results.

AUDIT STANDARDS

Standards for the use of platelet transfusions were obtained from respective BCSH guidelines on the use of platelet transfusions [3], transfusion guidelines for infants and older children [5], management of aplastic anaemia [6], management of acute myeloid leukaemia [7], diagnosis and management of immune thrombocytopenia [8], insertion of central access devices [9], and administration of blood components [10].

ORGANISATIONAL AUDIT

STANDARD 1.

"Local written guidelines should be available for the management of platelet transfusions in haematology patients".

[Recommendation from the previous audit. "Hospital Transfusion Committees must ensure there are written local guidelines for the use of platelets in all clinical specialities where platelet transfusions take place. As a minimum, these guidelines should be developed for platelet use in haematology,..."]

STANDARD 2.

Regular local audits should be performed to assess compliance with local guidelines.

[Recommendation from the previous audit. "Hospitals should carry out regular (at least annual) audits of compliance with these guidelines"]
[Ensure regular monitoring and audit of usage of red cells, platelets and fresh frozen plasma in all clinical specialities – HSC 2007/001 BBT – Safe and Appropriate Use of Blood][11]

CLINICAL AUDIT

STANDARD 1.

All patients should have a recent pre-transfusion platelet count checked prior to the platelet transfusion.

[According to the previous audit standards, this should be within 24 hours in in-patients and within 48 hours in out-patients].

STANDARD 2

2a.

The threshold for prophylactic platelet transfusions should be 10 x 10^9/L if the patient is an adult patient, with a reversible cause for bone marrow failure, who does not have any other risk factors for bleeding.

[BCSH Guidelines for the Use of Platelet Transfusions 2003 recommend a platelet count threshold of 10 x 10^9/L if the patient is stable. For patients without any risk factors, a threshold of 5 x 10^9／L may be appropriate if there are concerns that alloimmunization could lead to platelet refractoriness. However, accurate counting of low platelet numbers may create difficulties when trying to reduce the threshold below 10 x 10^9／L][3]

2b.

The threshold for prophylactic platelet transfusion in paediatric patients should be:

10 x 10^9/L
OR
20 x 10^9/L if:

- platelet count is expected to fall to < 10 x 10^9/L before next evaluation
- patient has severe mucositis
- patient has disseminated intravascular coagulation
- patient is on anticoagulant therapy
- patient has an increased risk of bleeding due to local tumour infiltration

[*BCSH Transfusion Guidelines for Neonates and Older Children 2004*] [5]

STANDARD 3

3a.

The threshold for prophylactic platelet transfusions should be 50 x 10^9/L prior to invasive procedures (gastroscopy and biopsy, liver biopsy, laparotomy, etc.) if the patient has no other risk factors for haemorrhage.

[*BCSH Guidelines for the Use of Platelet Transfusions 2003. For lumbar puncture, epidural anaesthesia, gastroscopy and biopsy, insertion of indwelling lines, transbronchial biopsy, liver biopsy, laparotomy or similar procedures, the platelet count should be raised to at least 50 x 10^9/L.*][3]

3b.

The threshold for prophylactic platelet transfusions should be 100 x 10^9/L prior to operations in critical sites such as the brain or eyes.

[*BCSH Guidelines for the Use of Platelet Transfusions 2003. For operations in critical sites such as the brain or eyes, the platelet count should be raised to 100 x 10^9/L*][3]

3c.

The threshold for prophylactic platelet transfusions should be 40 x 10^9/L prior to lumbar puncture or central line insertion in paediatric patients.

[*BCSH Transfusion Guidelines for Neonates and Older Children 2004. Indication for platelet transfusion is a platelet count 20 - 40 x 10^9/L prior to lumbar puncture and central line insertion.*][5]

STANDARD 4.

The post-transfusion platelet count should be checked prior to the procedure to ensure there has been a response to the platelet transfusion.

[*BCSH Guidelines for the Use of Platelet Transfusions 2003. It should not be assumed that the platelet count will rise just because platelet transfusions are given, and a preoperative platelet count should be checked to ensure that the desired thresholds have been reached.][3]*

STANDARD 5.

A platelet transfusion is not necessary prior to a bone marrow biopsy.

[*BCSH Guidelines for the Use of Platelet Transfusions 2003 recommend that bone marrow aspiration and biopsy may be performed in patients with severe thrombocytopenia without platelet support, providing that adequate surface pressure is applied*][3].

STANDARD 6.

Patients with immune thrombocytopenia or thrombotic thrombocytopenic purpura should only receive platelet transfusions if there is life-threatening bleeding.

[*BCSH Guidelines for the Use of Platelet Transfusions 2003. In immune thrombocytopenia platelet transfusions should be reserved for patients with life-threatening bleeding from the gastrointestinal or genitourinary tracts into the central nervous system or other sites associated with severe thrombocytopenia. In thrombotic thrombocytopenic purpura platelet transfusions are contraindicated unless there is life-threatening haemorrhage, as they have been temporarily associated with exacerbation of TTP.*][3]

STANDARD 7.

The rationale for the decision to give a platelet transfusion should be documented in the notes.

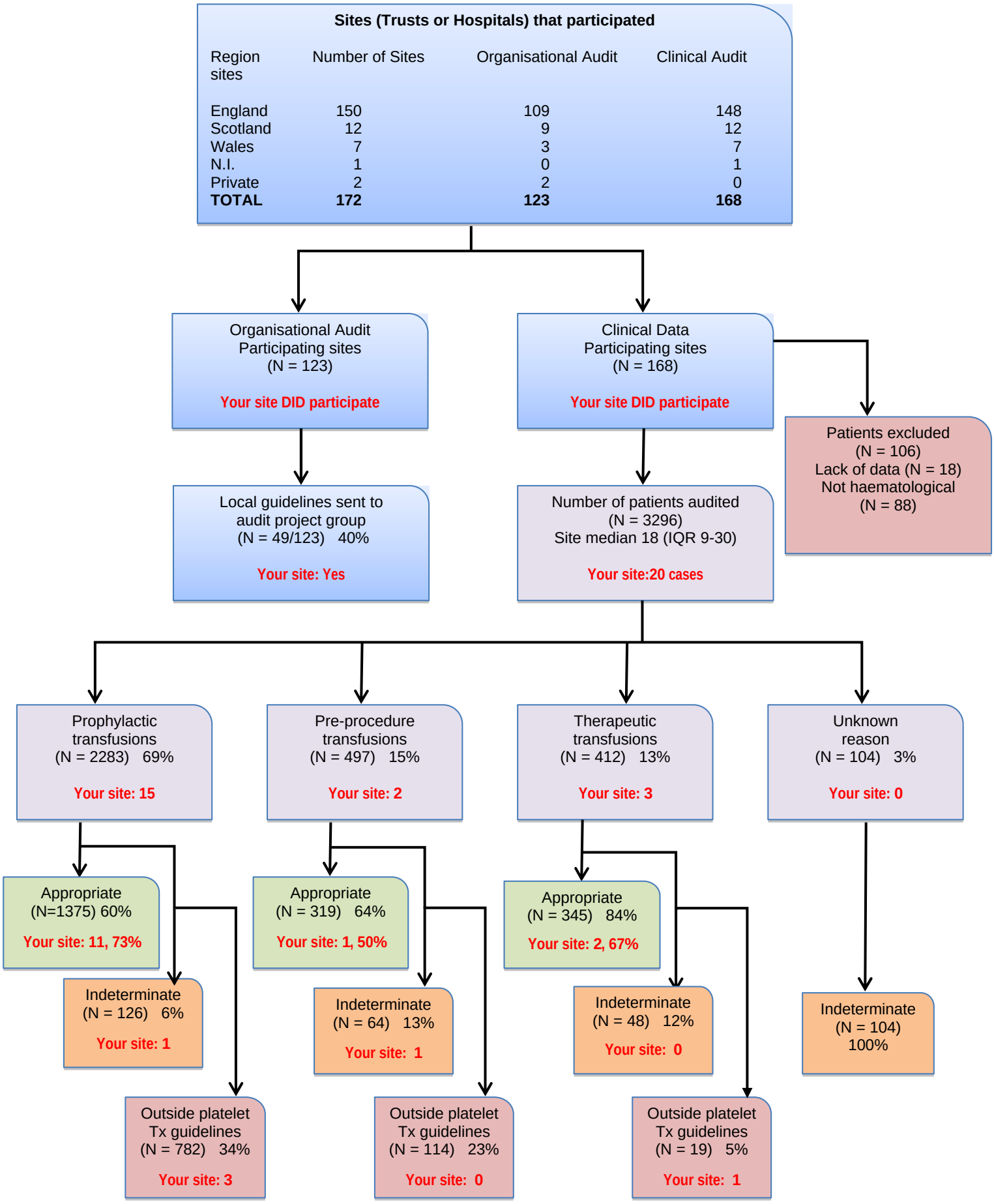
[*"The rationale for the decision to transfuse and the specific components to be transfused should be documented in the patient's clinical records." Administration of Blood Components BCSH guidelines 2009*][10]

["NHS Trusts should ensure that a minimum dataset for each transfusion is documented in the clinical notes (indication for transfusion; amount transfused; assessment of efficacy of transfusion; and any adverse effects and their management" HSC 2007/001 BBT Safe and Appropriate Use of Blood.][11]

RESULTS: AUDIT FLOW DIAGRAM

Sites (Trusts or Hospitals) that participated

Region sites	Number of Sites	Organisational Audit	Clinical Audit
England	150	109	148
Scotland	12	9	12
Wales	7	3	7
N.I.	1	0	1
Private	2	2	0
TOTAL	**172**	**123**	**168**



139/153 eligible trusts in England and North Wales[2] took part in this audit. A further 12 sites from Scotland, 7 from Wales, 1 from Northern Ireland and 2 from the private sector also took part.

A total of 172 sites[3] participated, 150 were within those areas supplied by NHSBT.

[2] NHSBT supplies hospitals in England & N. Wales.
[3] Sites submitted data either as individual hospitals or trusts; therefore the number of sites exceeds the number of eligible trusts. The number of eligible sites could not be estimated because whether data is submitted as a hospital or a trust varies from audit to audit.

RESULTS: ORGANISATIONAL AUDIT

YOUR SITE DID PARTICIPATE IN THE ORGANISATIONAL AUDIT

KEY POINTS

123 sites submitted organisational data of which 59% provided level 2b care or above. Excluding the 27 sites with no haematology beds, the median number of beds was 12 (inter-quartile range (IQR) 8 to 19).

96% (118/123) of sites indicated that written guidelines for haematology patients were available and in 88% (104/118) these were accessible on the hospital intranet.

Audit of platelet use was stated to occur in 50% (61/123) of sites, however in only 43% (26/61) of these had this occurred within the last 12 months.

Guidelines for adult and paediatric patients were the same at 101/123 sites, different at 18/123 sites and there were 4 paediatric patient only sites. No unique or common changes were apparent when paediatric guidelines were compared to adult, or combined adult and paediatric guidelines. Therefore, the data on the 119 adult or combined adult and paediatric guidelines were considered representative.

Guidelines relevant to adults (either adult only or combined with paediatric)

Prophylactic Platelet Transfusions

In patients with reversible bone marrow failure 98% (117/119) of sites use a threshold of 10 x 10^9/L

The majority of sites increased this threshold for situations considered to increase the risk of bleeding

- Most frequently stated threshold was 20 x 10^9/L.
- 31% (36/118) indicated that a threshold of 20 x 10^9/L would be applied to outpatients if the count was expected to fall below 10 x 10^9/L before the next evaluation.

Although BCSH guidelines do not recommend routine prophylactic platelet transfusions for stable patients with long term bone marrow failure, 36% (43/119) of sites indicated that these would be given at a count of either < 10 x 10^9/L or < 20 x 10^9/L.

Pre-procedure platelet transfusions

Most sites used BCSH guidelines to guide practice prior to invasive procedures with a usual threshold of 50 x 10^9/L, or 100 x 10^9/L for procedures involving the eyes or brain. An exception to this was for epidural anaesthesia where a more commonly stated threshold was 80 x 10^9/L.

Despite BCSH guidelines to the contrary, a significant minority of sites indicated that a platelet transfusion would be required if the platelet count was below a certain threshold prior to performing a bone marrow aspirate (12%) or a bone marrow aspirate and trephine (23%).

Guidelines relevant to paediatrics

There were no consistent differences between adult and paediatric guidelines.

Of note, the BCSH recommended threshold of 20 to 40 x 10^9/L prior to line insertion or lumbar puncture has not been widely adopted and was not used in any of the paediatric only hospitals.

Triage of requests

58% (71/123) of sites indicated that requests would be discussed with a haematology consultant or registrar.

Platelet wastage

Overall, in this audit, platelet wastage (5.8%) was double that of red cells (2.4%). When platelet wastage was assessed according to Blood Stocks Management Scheme (BSMS) usage categories there was a trend for higher wastage in low/very low usage sites (6.5%) compared to very high usage sites (4.3%).

Local blood centre information

Service level agreement blue light delivery time was greater than one hour for 64% (79/123) of sites. 22% (27/123) indicated that these delivery times affected practice. Comments identified that there was a balance to be struck between always having platelets available and transfusing strictly to guidelines, associated with high wastage, or accepting delays in provision and transfusing above the set threshold, to control wastage.

LOCAL GUIDELINES (STANDARD 1)

"Local written guidelines should be available for the management of platelet transfusions in haematology patients".

Guidelines were considered to be available if the reply indicated that these were accessible in written format, either as a paper copy or on the hospital intranet. In 5 sites written guidelines were not available. 28/118 sites with guidelines had separate paediatric and adult guidelines but in only 18 of these were there differences between the two. 49/118 sites provided local guidelines to the audit project team and 5 of these also contained paediatric guidelines. See table below.

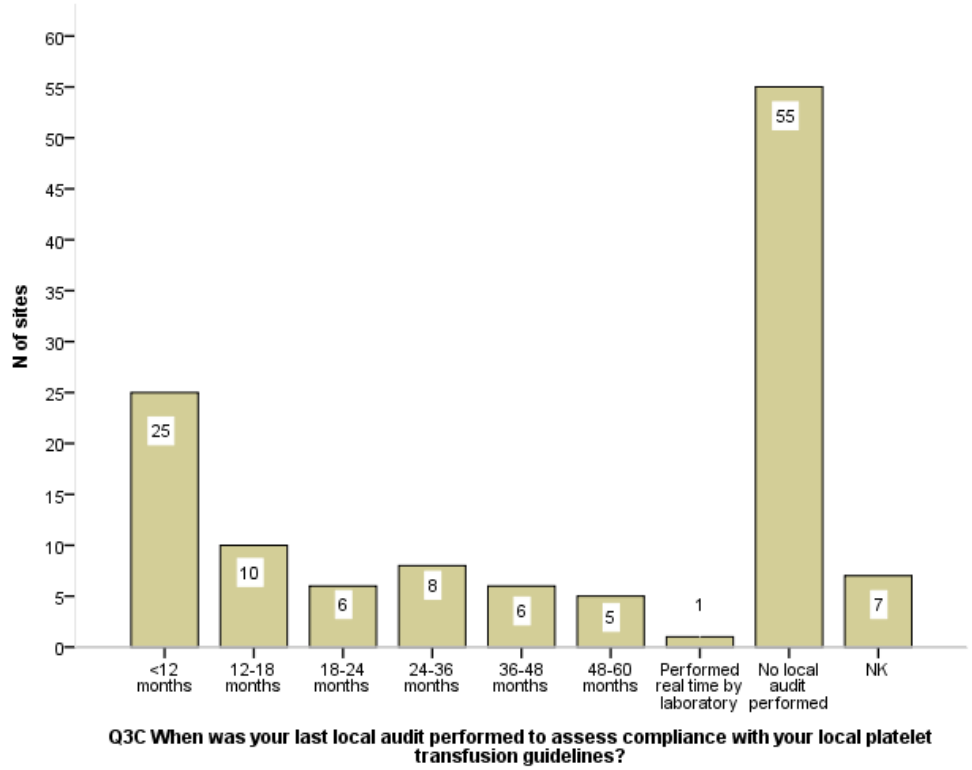
Do you have local written guidelines for the use of platelet transfusions in haematology patients?	**National (123 sites)**		**Your site**
	Number	**%**	
Yes	118	96	**Yes**
No	5	4	

LOCAL AUDITS (STANDARD 2)

Regular local audits should be performed to assess compliance with local guidelines.

50% (61/123) of sites indicated that local audit was performed, however in only 43% (26/61) of these was this within 12 months. See table and bar chart below.

Local audit performed to assess compliance with local platelet transfusion guidelines?	National (123 sites)		Your site
	Number	%	
YES, performed	61	50	
NO, not performed	55	45	YES, <12M
Not known	7	6	



Q3C When was your last local audit performed to assess compliance with your local platelet transfusion guidelines?

GUIDELINES FOR PLATELET TRANSFUSION

Three distinct types of site were identified:

Type A - 101 sites with either adult only, or combined adult and paediatric guidelines.
Type B - 18 sites where the paediatric guidelines were different to those for adults.
Type C - 4 Paediatric only sites.

Your site was classed as being TYPE A

Adult guidelines: The national results are summarised for all 119 sites that have guidelines relevant to adults either separate or combined with paediatric guidelines.

Paediatric guidelines: The national results in the paediatric section relate to the 34 sites with separate paediatric guidelines. This includes data from: 12 sites where guidelines were separate to adult guidelines but not different; 18 sites where there were differences between adult and paediatric guidelines; and 4 paediatric sites.

No unique or common changes were apparent when paediatric guidelines were compared to adult or combined adult and paediatric guidelines.

NB: - 'Your Site data' is given in the adult section for ALL 123 participating sites, i.e. including the 4 TYPE C Paediatric-only sites. 'Your Site data' is only reported for adult guidelines for TYPE B sites.

GUIDELINES FOR PROPHYLACTIC PLATELET TRANSFUSIONS

Platelet transfusion threshold in patients with no additional risk factors for bleeding with a reversible cause of bone marrow failure.

Guidelines relevant to adults (either combined or separate to paediatric)

98% (117/119) of sites indicated that a platelet threshold of 10 x 10^9/L would be used. See table below.

What is your current threshold for prophylactic platelet transfusions (i.e. in the absence of bleeding) in patients who have no additional risk factors for bleeding and have a reversible cause of bone marrow failure?	National (119 sites) Number	%	Your site
<10 x 10^9/L	117	98	
<20 x 10^9/L	1	1	**<10**
Other*	1	1	

*No specified threshold, clinical basis

Guidelines relevant to paediatrics only

88% (30/34) of sites indicated that a platelet threshold of 10 x 10^9/L would be used.

What is your current threshold for prophylactic platelet transfusions (i.e. in the absence of bleeding) in patients who have no additional risk factors for bleeding and have a reversible cause of bone marrow failure?	National (34 sites) Number	%
<10 x 10^9/L	30	88
<20 x 10^9/L	2	6
Other (No specified threshold, clinical basis)	2	6

Additional risk factors for prophylactic transfusion

Guidelines relevant to adults (either combined or separate to paediatric)

In keeping with BCSH guidelines, the majority of sites increased their usual platelet threshold in the presence of most situations considered to increase the risk of bleeding. See table below.

Does your prophylactic threshold change if patient:	National (119 sites)						Your site
	YES, threshold changes		Number changing to:			Other change	
	Number	%	20	30	50		
5. has Acute Promyelocytic Leukaemia (APL)	79/111	71	43	5	22	9	YES, <20
6. is having a stem cell transplant	1/56	2	1	-	-	-	No change
7. has a fever	106	89	100	-	1	5	YES, <20
8. has an infection	93	78	82	-	-	11	YES, <20
9. has Disseminated Intravascular Coagulation (DIC)	96	81	42	-	30	24	No change
10. is taking therapeutic anticoagulant drugs	80	67	17	9	37	17	YES, <20
11. is taking therapeutic anti-platelet agents	44/116	38	28	2	9	5	YES, <20
12. has had a previous significant bleed	73/117	62	28	-	14	31	No change
13. is receiving Anti-Thymocyte Globulin (ATG)	52/118	44	20	14	11	7	YES, <20
14. is taking therapeutic antifungal drugs	33/117	28	31	-	1	1	No change
15. is an outpatient and platelet count is expected to fall to <10 x 10^9/L before the next evaluation	54/118	46	36	-	-	18	No change
16. Other factors that change local threshold	29/110	26	8	3	4	14	No change

This summary table excludes sites from the denominator if the information was not known (NK) or the question was said to be not applicable (NA). Thus, the table denominator is 119 unless stated.

The most frequently stated threshold change was to 20 x 10^9/L. Exceptions to this were: patients on therapeutic anticoagulation where the most common was 50 x 10^9/L; and patients with a previous bleed where "other" was the most common category. The "other" category contained rationale statements such as the actual threshold would depend upon the site, severity and platelet count at which the bleed occurred.

In contrast to most situations where an increased threshold was applied, this was not the case for patients receiving ATG or therapeutic antifungal agents where only 44% (52/118) and 28% (33/117) of sites respectively indicated that an increased threshold would be used.

In patients receiving ATG the most common threshold change was to 20 x 10^9/L despite a threshold of 30 x 10^9/L being recommended in BCSH guidelines for the management of aplastic anaemia [5].

Of those who specified that no change in threshold would be applied to patients on antiplatelet drugs, 10 indicated that the drug would be stopped.

31% (36/118) of sites indicated that a threshold of 20 x 10^9/L would be applied to outpatients if the count was expected to fall below 10 x 10^9/L at the next evaluation. As this indication is included in the BCSH guidelines for neonates and older children it is likely to represent a rationalisation of disparate guidelines at sites where common adult and paediatric guidelines are applied.

89% (106/119) of sites increased their threshold if a patient has a fever. Fever is not mentioned specifically in the BCSH guidelines [3] as a reason to increase the transfusion threshold[4], although it is mentioned in the aplastic anaemia guidelines [6]. There was significant variability in what constituted a fever. In 10 no definition of fever was stated and in others this either involved a single temperature threshold (68/96), a sustained temperature threshold (14/96), or a combination of both (14/96) (See Appendix 5). The sustained definitions were typically of 2 readings at least one hour apart. Almost half of local definitions (46%, 44/96) comprised a single temperature threshold of 38.0 degrees with no sustained temperature.

93 sites indicated infection would result in a threshold change. In 14 of these no definition was provided. In the remaining 79 replies 77% (61) included symptoms, 11% (9) included signs, 52% (41) included treatment with antimicrobials and 27% (21) included the presence of proven infection.

Other factors changing local threshold guidelines are detailed in Appendix 4.

Guidelines relevant to paediatrics only

In keeping with BCSH guidelines, the majority of sites increased their usual platelet threshold in the presence of most situations considered to increase the risk of bleeding. See table below.

Generally there was consistency between adult and paediatric guidelines.

33% (11/33) of sites indicated that a threshold of 20 x 10^9/L would be applied to outpatients if the count was expected to fall below 10 x 10^9/L at the next evaluation. Of the 4 paediatric hospitals which took part in the audit, only one said that their threshold would change if the platelet count was expected to fall to < 10 x 10^9/L before the next evaluation. This is in contrast to the recommendations from BCSH [5].

[4] However, it may be a rationalisation of the landmark platelet transfusion trial {, #223} protocol that used a threshold of 20 x 10^9/L if the patient's temperature was 38^{o}C or higher.

Does your prophylactic threshold change if patient:	National (34 sites) YES, threshold changes		Number changing to:					Other change
	Number	%	10	20	30	50	75	
5. has Acute Promyelocytic Leukaemia (APL)	17/32	53	-	10	1	5	-	1
6. is having a stem cell transplant	2/20	10	-	2	-	-	-	-
7. has a fever	29	85	1	23	1	-	-	4
8. has an infection	27	79	1	22	1	1	-	2
9. has Disseminated Intravascular Coagulation (DIC)	27	79	-	6	1	14	-	6
10. is taking therapeutic anticoagulant drugs	21/32	66	-	2	1	15	1	2
11. is taking therapeutic antiplatelet agents*	14/31	45	-	6	1	4	-	3
12. has had a previous significant bleed	27	79	-	3	1	8	1	13
13. is receiving Anti-Thymocyte Globulin (ATG)	13/33	39	-	3	6	3	-	1
14. is taking therapeutic antifungal drugs	6/32	19	-	5	-	-	-	1
15. is an outpatient and platelet count is expected to fall to $<10 \times 10^9$/L before the next evaluation	18/33	55	-	11	-	-	-	7
16. Other factors that change local threshold*	15/32	47	-	1	6	4	-	4

This summary table excludes sites from the denominator if the information was not known (NK) or the question was said to be not applicable (NA). Thus, the table denominator is 34 unless stated.

Q6. For the two sites with changes in threshold, autologous, allogeneic full intensity and allogeneic reduced intensity transplants were affected by the change.
*Q16: Other factors were: CNS tumour (4); Neonate (2); ITU (1); BMT for sickle cell disease (1); dysfunctional platelets (1); clinical judgement (3).

Platelet transfusion in patients with long term bone marrow failure

Guidelines relevant to adults (either combined or separate to paediatric)

Despite BCSH guidelines which do not recommend routine prophylactic platelet transfusion for patients with long term bone marrow failure 36% (43/119) of all sites indicated that these would be given at a count of either < 10 x 10^9/L or < 20 x 10^9/L. See table below.

Do you give routine prophylactic platelet transfusions to stable patients (i.e. not bleeding/ no infection) with long term bone marrow failure e.g. patients with myelodysplasia?	National (119 sites) Number	%	Your site
YES	44	37	
Threshold, if YES:			
<20 x 10^9/L	7		YES, <10
<10 x 10^9/L	36		
Other*	1		

* On an individual patient basis

Guidelines relevant to paediatrics only

Despite BCSH guidelines which do not recommend routine prophylactic platelet transfusion for patients with long term bone marrow failure 36% (12/33) of sites indicated that these would be given at a count of < 10 x 10^9/L. See table below.

Do you give routine prophylactic platelet transfusions to stable patients (i.e. not bleeding/ no infection) with long term bone marrow failure e.g. patients with myelodysplasia?	National (33 sites) Number	%
YES	14	42
Threshold, if YES:		
<20 x 10^9/L	1	
<10 x 10^9/L	12	
Other*	1	

*On an individual patient basis

Of the 4 paediatric hospitals which took part in the audit. Only one site indicated that a platelet threshold would be used to determine platelet transfusion in patients with stable long term bone marrow failure.

GUIDELINES FOR PRE-PROCEDURE PLATELET TRANSFUSIONS

Threshold platelet count pre-procedure

Guidelines relevant to adults (either combined or separate to paediatric)

BCSH guidelines recommend that a threshold of at least 50 x 10^9/L be used to guide the need for platelet transfusion prior to most procedures. Exceptions to this are: –

- Bone marrow aspiration and biopsy which may be performed without platelet support, providing that adequate surface pressure is applied [3]
- Operations in critical sites such as the brain or eyes, where the platelet count should be raised to 100 x 10^9/L [3]
- Guidelines for ITP which recommend a threshold of 80 x 10^9/L for epidural anaesthesia [8]

The majority of replies indicated that local guidelines were in keeping with the above recommendations. See table below.

Threshold platelet counts for specific procedures (119 sites)

Procedure	Platelet Tx Not required	Platelet count threshold*										Not stated	Your site
		10	20	30	40	50	70	75	80	100	Other**		
Bone marrow aspirate	92	2	2	1	-	9	-	-	-	-	-	13	**Not required**
Bone marrow aspirate & Trephine	78	2	8	2	1	13	-	-	1	-	-	14	**Not required**
Endoscopy alone	39	-	2	2	-	56	-	-	-	-	-	20	**Not required**
Endoscopy & biopsy	3	-	-	-	-	90	-	-	11	1	-	14	**50**
Insertion of indwelling line	4	--		-	-	102	-	-	8	-	-	5	**Not required**
Lumbar puncture	1	-	1	-	1	79	1	1	22	8	1	4	**50**
Epidural anaesthetic	1	-	-	-	-	42	1	1	51	13	1	9	**50**
Liver biopsy or other organ biopsy	-	-	-	-	-	63	1	2	34	11	1	7	**50**
Surgery excluding eye or brain	2	-	-	-	-	60	-	1	33	15	1	7	**50**
Surgery of eye or brain	-	-	-	-	-	2		-	7	101	-	9	**100**

* Platelet count options of <50, <80 & < 100 were stated on the questionnaire, and for clarity of presentation the table has been expanded to include some of the other platelet count options that were stated.

** Other options comprised "specialist guidelines" (lumbar puncture, epidural, liver biopsy), "50/80/100" (surgery excluding eye or brain).

For epidural anaesthesia 35% (42/119) indicated a threshold of 50 x 10^9/L and 43% (51/119) indicated that a threshold of 80 x 10^9/L would be used.

There are no guidelines for endoscopy without biopsy and replies identified that 33% (39/119) would not transfuse platelets but 47% (56/119) would use a threshold of 50 x 10^9/L

Despite BCSH guidelines to the contrary, a significant minority of sites indicated that a platelet transfusion would be required if the platelet count was below a certain threshold, prior to performing a bone marrow aspirate (12%, 14/119) or a bone marrow aspirate and trephine (23%, 27/119).

Guidelines relevant to paediatrics only

Generally thresholds for procedures were similar when adult and paediatric guidelines were compared, with similar deviations from national guidelines.

Despite BCSH guidelines to the contrary, a significant minority of sites indicated that a platelet transfusion would be required if the platelet count was below a certain threshold, prior to performing a bone marrow aspirate (18%, 6/34) or a bone marrow aspirate and trephine (35%, 12/34). Of the 4 paediatric hospitals which took part in the audit, one site indicated that a threshold of 50 x 10^9/L would be used prior to bone marrow aspirate and trephine.

In paediatric patients a platelet transfusion threshold of 20 to 40 x 10^9/L is recommended for insertion of indwelling lines and lumbar puncture [5]. None of the hospitals followed this recommendation. 9% (3/34) of sites followed this recommendation for lumbar puncture.

Threshold platelet counts for specific procedures (34 sites)

Procedure	Platelet Tx Not required	Platelet count threshold*								
		10	20	30	40	50	80	100	Other	Not stated
Bone marrow aspirate	24	1	2	-	-	3	-	-	-	4
Bone marrow aspirate & Trephine	19	2	3	1	-	6	-	-	-	3
Endoscopy alone	10	-	3	-	-	16	-	-	-	5
Endoscopy & biopsy	2	-	1	-	-	21	4	1	-	5
Insertion of indwelling line	1	-	-	-	-	29	1	2	-	1
Lumbar puncture	1	-	2	-	1	23	3	2	1	1
Epidural anaesthetic	-	-	1	-	-	10	17	4	1	1
Liver biopsy or other organ biopsy	-	-	1	-	-	18	8	4	1	2
Surgery excluding eye or brain	-	-	-	-	-	17	9	6	-	2
Surgery of eye or brain	-	-	-	-	-	1	3	28	-	2

* Platelet count options of <50, <80 & < 100 were stated on the questionnaire, and for clarity of presentation the table has been expanded to include some of the other platelet count options that were stated.

OTHER RESULTS IN DETAIL

BCSH LEVEL OF CARE OF HOSPITALS INVOLVED IN AUDIT

59% (73/123) of all sites who participated in the audit treat patients with intensive, complex chemotherapy regimens which would be expected to result in frequent severe thrombocytopenia. See table below.

What level of haematology care does your hospital provide (according to BCSH criteria)?	National (123 sites)		Your site
	Number	%	
Level 1	20	16	
Level 2a	29	24	
Level 2b	32	26	Level 2b
Level 3	41	33	
Not known	1	1	

NUMBER OF DESIGNATED HAEMATOLOGY BEDS

120 out of 123 sites provided information. Excluding 27 sites that did not have any designated haematology beds the median number of beds was 12, IQR 8 to 19, and range 4 to 59.

ACCESS TO GUIDELINES

88% (104/118) of participants indicated that guidelines were available on the hospital intranet. Other common places where these were accessible included at doctors' induction teaching sessions (39% (46/118)) and in guideline or protocol folders on wards 36% (42/118).

LOCAL BLOOD CENTRE

Service level agreement Blue Light Delivery times

64% (79/123) of all sites have delivery times of more than one hour. 27 stated that this affected transfusion practice and common themes included: –

- Lower threshold for platelet requests
- Pre-order for presumed transfusion of known patients
- Stock platelets with either accepted wastage or transfusion above stated threshold
- Delayed administration

See tables below

What is your stated Service Level Agreement Blue Light delivery time?	National (123 sites)		Your site
	Number	%	
46-60 minutes	36	29	
61-90 minutes	33	27	
91-120 minutes	39	32	
121-180 minutes	7	6	**46-60m**
>180 minutes	0	0	
No stated Agreement	2	2	
Not known	6	5	

Does this blue light delivery time affect your transfusion practice?	National (123 sites)		Your site
	Number	%	
Yes	27	22	
No	90	73	**No**
Not known	6	5	

BLOOD STOCKS

Sites were asked for the numbers of platelets and red blood cell units requested, used and wasted, during the stock year 1 April 2009 to 31 March 2010. On analysing the data it was clear that the term "requested" may have been interpreted to include allocated stock which was then re-issued. For this reason "requested" data has been omitted from analysis.

The tables below summarise information from 100 sites who submitted both total used and wasted data for red cells and platelets.

Proportion of platelets wasted

Platelet used and wasted data	National (100)	Your site
Median (IQR) stated as "used"	766 (368 to1449)	**744**
Median (IQR) stated as "wasted"	43 (22 to 89)	**55**
Median (IQR) of wasted as % of total	5.8% (3.6 to 8.9%)	**6.9%**

Proportion of RBC wasted

Red cell used and wasted data	National (100)	Your site
Median (IQR) stated as "used"	7624 (5123 to 11717)	**9050**
Median (IQR) stated as "wasted"	171 (111-358)	**201**
Median (IQR) of wasted as % of total	2.4% (1.5 to 3.5%)	**2.2%**

Overall platelet wastage was more than double that of red cells. When platelet wastage was assessed according to BSMS usage categories for sites, median wastage was 4.3% with very high usage (N = 21), 5.8% with high usage (N = 24), 6.5% with moderate usage (N = 20), 6.5% with low/very low usage (N = 18) and 8.4% for sites where the usage category was unknown (N = 17).

TRIAGE OF REQUESTS

58% (71/123) of sites indicated that requests were discussed with a haematology consultant or registrar. It is not clear whether all requests or only those outside of guidelines are included.

7-DAY PLATELET TRIAL

Only 7 sites indicated that they were involved in the 7 day platelet trial. Stocking of platelets for this purpose and wastage is therefore unlikely to have a significant effect in this audit.

RESULTS: CLINICAL AUDIT

YOUR SITE DID PARTICIPATE IN THE CLINICAL AUDIT
20 case(s) were analysed

KEY POINTS

Clinical data was submitted from 3402 transfusion episodes of which 3296 were analysed. 106 cases were excluded due to lack of data or because the patient did not have a haematological diagnosis. 60% of included cases were aged 60 years or over and 7% were under 18 years.

68% were in-patients and most (74%) were given the platelet transfusion on a haematology ward. 32% were out-patients and most (82%) were given the platelet transfusion on a haematology day unit.

The most common underlying haematological diagnoses were acute myeloid leukaemia (29%), lymphoma (19%) and myelodysplasia (11%).

A pre-transfusion count was performed in 98% (3232/3296) of cases however in only 92% (3046/3296) was this within 24 hours if an inpatient or 48 hours if an outpatient.

Although the reason for the transfusion was clearly documented in the notes in only 72% of cases, auditors were able to identify the reason for transfusion in 97% of cases. This was prophylactic in 69% (2283/3296), pre-procedure in 15% (497/3296), therapeutic in 13% (412/3296) and unclear in 3% (104/3296).

Prophylactic platelet transfusions (2283 cases)

Adults - 2132 cases. 34% were given when the pre-transfusion platelet count was $\leq 10 \times 10^9$/L

Paediatrics - 151 cases (Aged ≤ 18yrs of age). 23% were given when the pre-transfusion platelet count was $\leq 10 \times 10^9$/L. A further 18% were clearly compliant with BCSH guidelines for prophylactic platelet transfusions in paediatric patients which specifies alternative thresholds for specific risk factors in paediatric patients.

Using an algorithm (See Appendix X) to further evaluate appropriateness of transfusion (based on the platelet count and timing, BCSH guidelines, documentation of an increased bleeding risk and whether platelet units were due to expire on the day of transfusion) 60% were found to be appropriate. The number of appropriate transfusions was higher in paediatric cases than adult cases at 74% and 59% respectively.

Pre-procedure platelet transfusions (497 cases)

The most common procedures for which a platelet transfusion was given were line insertion (28%) followed by surgery not involving the eye or brain (23%).

In only 81% of cases was the transfusion given within 6 hours of the procedure.

Only 30% of cases had the post-transfusion platelet count checked prior to the procedure.

In 9% of cases (45/497) the only procedure performed was a bone marrow aspirate and/or trephine biopsy.

Using an algorithm to further evaluate appropriateness of transfusion (based on the platelet count and timing, the diagnosis, BCSH guidelines and whether an individual safe platelet threshold was documented) 64% were found to be appropriate.

Excessive bleeding was reported in 5% of cases in the 24 hours following the procedure. 14 of these had surgical procedures and these accounted for: 75% of cases with haemodynamic compromise; 70% of cases needing extra red cell or platelet support; and all cases who required additional surgery.

Therapeutic platelet transfusions (412 cases)

The most common types of bleeding were nose bleeds, malaena and large or multiple bruises.

Using an algorithm to assess appropriateness for both adult and paediatric cases (based on the diagnosis, and severity of bleeding) 84% (345/412) were considered appropriate and 5% (19/412) outside of platelet guidelines. All 19 cases who were classified as outside of guidelines had ITP with non-life-threatening bleeding.

In 18% (73/412) of cases the bleeding caused haemodynamic compromise. In 58% (239/412) the bleeding stopped following the audited transfusion but in 39% (159/412) bleeding continued.

Complications of transfusion

1% (42/3296) of all cases were considered to have had a reaction to the platelet transfusion. 6 were reported as febrile reactions with other symptoms/signs, 3 were isolated febrile reactions, 32 were allergic (30 minor but 2 severe) and 1 developed hypotension.

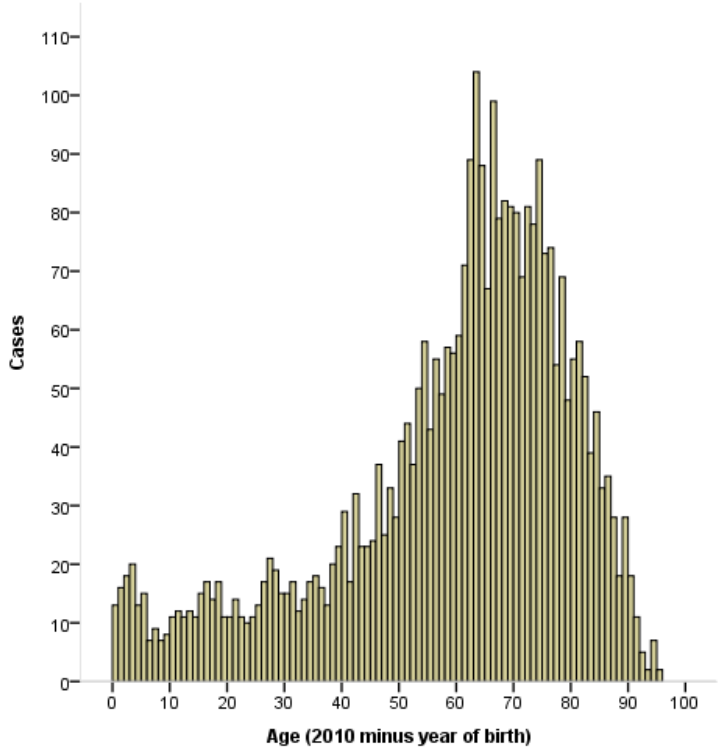
Information about platelets transfused

Using a conservative estimate - 46% of total platelets issued to participating sites over the audited period were used by the audited cases. In 23% of cases (764/3296) at least one unit was due to expire at midnight on the day of transfusion.

BASELINE CHARACTERISTICS OF PATIENTS

The median age was 64 years, IQR 49 to 74 years and range 0 to 95 years. 7% (229/3296) of cases were aged under 18 years and 60% (1971/3296) were aged 60 years or over. See histogram below.

Age of patients



59% (1948) were men and 41% (1347) were women.

In adults the median weight was 73kg, IQR 63 to 85kg. In paediatric cases the median weight was 24kg, IQR 15 to 47kg.

68% (2225/3296) of all cases were inpatients [66% (2024/3067) adult and 88% (201/229) paediatric] and 32% (1071/3296) were outpatients.

74% (1636/2225) of inpatient transfusions were given on haematology wards with the majority of others (15% (344/2225)) given on medical admissions/medical wards. In only 5% (116/2225) was the admission solely for the administration of platelets.

82% (875/1071) of outpatient transfusions were given on a designated haematology day unit with the majority of others (15% (166/1071)) given on medical or oncology day units.

HAEMATOLOGICAL DIAGNOSIS

Haematological Diagnosis	National (3296 cases)		Your site
	Number	%	Number
Acute lymphocytic leukaemia	211	6.4	1
Acute myeloid leukaemia excluding M3	921	27.9	7
Acute promyelocytic leukaemia (M3)	41	1.2	1
Aplastic anaemia	173	5.2	2
Burkitt's lymphoma	35	1.1	
Chronic lymphocytic leukaemia (CLL)	139	4.2	1
Chronic myeloid leukaemia (CML)	62	1.9	
Diffuse large b cell lymphoma (DLBCL)	159	4.8	2
Follicular lymphoma	59	1.8	
Hodgkin's lymphoma (HL)	101	3.1	
Immune thrombocytopenic purpura (ITP)	105	3.2	3
Myelodysplasia	364	11.0	1
Myelodysplastic/myeloproliferative Neoplasms (includes CMML,JMML)	74	2.2	
Myeloma/plasma cell dyscrasia	296	9.0	
Myeloproliferative neoplasms including Myelofibrosis	54	1.6	
Thrombotic thrombocytopenic purpura (TTP)	10	.3	
Other acute leukaemia	37	1.1	
Other chronic leukaemia	13	.4	
Other lymphoma	263	8.0	2
Other (others)*	179	5.4	

The most common diagnoses were acute myeloid leukaemia (29%), lymphoma (18%) and myelodysplasia (11%). Category "other" included patients with haemoglobinopathies, familial thrombocytopenia, platelet function disorders, Fanconi's anaemia, haemophagocytic lymphohistiocytosis and other rare haematological conditions. In 49 cases no haematological diagnosis or other diagnosis was reported and 46 cases had a diagnosis of either pancytopenia or thrombocytopenia.

GENERAL STANDARDS

STANDARD 1

All patients should have a recent pre-transfusion platelet count checked prior to the platelet transfusion. *[According to the previous audit standards, this should be within 24 hours in in-patients and within 48 hours in out-patients].*

A pre-transfusion platelet count was performed in 98% (3232/3296) of all cases. However, in only 92% (3046/3296) was this within 24 hours if an inpatient or 48 hours if an outpatient. Only 18% (44/250) of those patients who did not have a recent pre-transfusion platelet count had a diagnosis of MDS. See table below.

Was a platelet count performed within 24 hours of the platelet transfusion if the patient was an inpatient, or within 48 hours of the platelet transfusion if the patient was an out-patient? %YES	National		**Your site**	
	Number	%	**Number**	**%**
All cases	3046/3296*	92	**18/ 20**	**90**
Inpatient	2130/2225*	96	**7/ 7**	**100**
Outpatient	916/1071*	86	**11/ 13**	**85**

*denominator includes 12 inpatient and 26 outpatient cases for whom Q17 was not known.

STANDARD 7

The rationale for the decision to give a platelet transfusion should be documented in the notes.

The rationale for the decision to give a platelet transfusion should be documented in the notes.	National (3296 cases)		**Your site (20 cases)**	
	Number	%	**Number**	**%**
Indication documented	2386	72	**20**	**100**
Indication NOT documented	910	28	**0**	**0**

In only 72% of cases was the indication for the platelet transfusion clearly documented in the notes. However, in 97% (3192/3296) of cases the auditor was able to determine from the patient's records whether this was for prophylaxis, pre-procedure or therapeutic - as below.

Reason for platelet transfusion determined by auditor	National (3296 cases)		**Your site (20 cases)**	
	Number	%	**Number**	**%**
Prophylactic platelet transfusion patient not bleeding and not having a procedure	2283	69	**15**	**75**
Pre procedure platelet transfusion no significant bleeding	497	15	**2**	**10**
Therapeutic platelet transfusion significant bleeding	412	13	**3**	**15**
Reason for transfusion not clear from patient records	104	3.2	**0**	**0**

PROPHYLACTIC PLATELET TRANSFUSIONS

69% (2283/3296) of all cases received a prophylactic platelet transfusion.

ADULT CASES (STANDARD 2)

The threshold for prophylactic platelet transfusions should be 10 x 10^9/L if the patient is an ADULT PATIENT, with a reversible cause for bone marrow failure, who does not have any other risk factors for bleeding.

	National		Your site	
	Number	%	Number	%
Was the pre-transfusion platelet count ≤10 x 10^9 per L AND does the patient have a reversible cause of bone marrow failure? (e.g. The patient is being actively treated for a haematological disorder, is receiving chemotherapy or stem cell transplants). **% YES**	715/2132	34	**11/ 14**	**79**

2132 out of 2283 replies were for adult patients. 34% (715/2132) had a platelet count of ≤ 10 x 10^9/L. In a further 38% (815/2132) of cases reasons for transfusion outside of the usual threshold were documented in the notes. See tables below.

Number of patients with reasons for transfusion outside of guidelines

	National		Your site	
	Number	%	Number	%
If the platelet count was not ≤10 x 10^9 per L was a reason specified in the notes for why the patient was given the platelet transfusion outside of the current guidelines ? **% WITH REASON GIVEN**	815/1417	58	**2/ 3**	**67**

What were the reasons for transfusion outside current guidelines:-

Please state the reason(s) documented in the notes (for why the patient was given the platelet transfusion outside of the current guidelines) *(Tick as many as apply)*		National		Your site
		Number	% of reasons given (1150)	Number
Severe mucositis		28	2.4	**0**
Severe leucocytosis (WCC > 75)		30	2.6	**0**
Infection	Fever ≥ 38C	197	17.1	**0**
	Systemic infection e.g. pneumonia, septicaemia	188	16.3	**0**
	Treatment with therapeutic antifungals e.g. Ambisome/ Amphocil/ Amphotericin B	33	2.9	**0**
Bleeding diathesis	Treatment with anticoagulants	35	3.0	**1**
	Treatment with antiplatelet agents	6	0.5	**0**
	Treatment with Anti-thymocyte globulin (ATG)	10	0.9	**0**
	Inherited bleeding problem e.g. haemophilia, von Willebrand's disease, platelet function disorder	3	0.3	**0**
	Acquired bleeding disorder (not associated with medication or promyelocytic leukaemia) e.g. Disseminated Intravascular Coagulation (DIC)	11	1.0	**0**
	Coagulopathy associated with promyelocytic leukaemia	9	0.8	**0**
Increased bleeding risk	Recent major operation (i.e. within the previous 2 weeks)	5	0.4	**0**
	Previous significant haemorrhage	62	5.4	**1**
Pregnant		0	0	**0**
Platelet count expected to fall < 10 x 10^9/L before next evaluation		366	31.8	**0**
Other *		167	14.5	**0**

*Other category included minor bleeding (38), history of recurrent bleeding (19), to reduce frequency of visits (12), minor infection/procedure/illness (13), possible bleeding (10), chemotherapy (10), treatment with Bortezomib (9) liver dysfunction (1) and hazardous job (1).

PAEDIATRIC CASES (STANDARD 2)

The threshold for prophylactic platelet transfusion in paediatric patients should be:
10 x 10^9/L
OR
20 x 10^9/L if:

- platelet count is expected to fall to < 10 x 10^9/L before next evaluation
- patient has severe mucositis
- patient has disseminated intravascular coagulation
- patient is on anticoagulant therapy
- patient has an increased risk of bleeding due to local tumour infiltration

151 out of 2283 replies were for paediatric patients. 40% (34 + 27 = 61/151) of cases were clearly compliant with BCSH guidelines for prophylactic platelet transfusions in paediatric patients. In a further 30% (46/151) of cases reasons for transfusion outside of the usual threshold were documented in the notes. See tables below.

	National		Your site (1 cases)	
	Number	%	Number	%
Was the pre-transfusion platelet count ≤10 x 10^9 per L AND does the patient have a reversible cause of bone marrow failure? (e.g. The patient is being actively treated for a haematological disorder, is receiving chemotherapy or stem cell transplants). **% YES**	34/151	23	**0/ 1**	**0**

	National		Your site
	Number	%	Number
If the platelet count was not ≤10 x 10^9/L was a reason specified in the notes for why the patient was given the platelet transfusion outside of the current guidelines ? **% WITH REASON GIVEN**	73/117	62	**1/ 1**
For those 73 with a reason given in the notes:			
Platelet count was ≤20 x 10^9/L	47/73	64	**1**
Platelet count was ≤20 x 10^9/L AND ONE OR MORE of the following was present:	27/73	37	**0**
• platelet count is expected to fall to < 10 x 10^9/L before next evaluation	25/47		
• patient has severe mucositis	2/47		
• patient has disseminated intravascular coagulation	1/47		
• patient is on anticoagulant therapy	0/47		
• patient has an increased risk of bleeding due to local tumour infiltration	0/47		

What were the reasons for the remaining 46 (73–27) PAEDIATRIC patients being transfused outside of current guidelines:-

Please state the reason(s) documented in the notes (for why the patient was given the platelet transfusion outside of the current guidelines) *(Tick as many as apply)*		National		Your site
		Number	% of 58 reasons	Number
Severe mucositis		2	3	**0**
Severe leucocytosis (WCC > 75)		3	5	**0**
Infection	Fever ≥ 38C	20	34	**1**
	Systemic infection e.g. pneumonia, septicaemia	9	16	**0**
	Treatment with therapeutic antifungals e.g. Ambisome/ Amphocil/ Amphotericin B	5	9	**0**
Bleeding diathesis	Treatment with anticoagulants	1	2	**0**
	Treatment with antiplatelet agents	1	2	**0**
	Treatment with Anti-thymocyte globulin (ATG)	0	0	**0**
	Inherited bleeding problem (e.g. haemophilia, von Willebrand's disease, platelet function disorder	0	0	**0**
	Acquired bleeding disorder (not associated with medication or promyelocytic leukaemia) [e.g. Disseminated Intravascular Coagulation (DIC)]	0	0	**0**
	Coagulopathy associated with promyelocytic leukaemia	0	0	**0**
Increased risk of bleeding	Recent major operation (e.g. within the previous 2 weeks)	0	0	**0**
	Previous significant haemorrhage	1	2	**0**
Pregnant		0	0	**0**
Platelet count expected to fall < 10 x 10^9/L before next evaluation		4	7	**0**
Other *		12	21	**1**

*Other category included history of recurrent bleeding (2), coagulation abnormality (1), increased risk of bleeding (1), aplastic anaemia (1), and neonatal alloimmune thrombocytopenia (NAIT) (1).

ALGORITHM

To further evaluate the appropriateness of transfusion in both adult and paediatric cases a prophylactic platelet transfusion algorithm was devised (Appendix 1) which considered - the pre-transfusion platelet count, the time at which this was performed, BCSH guidelines which recommend a threshold platelet count or allow an increased threshold for specific situations considered to have a greater bleeding risk, and whether platelet units were due to expire on the day of transfusion.

Using this algorithm 56% (1281/2283) of all platelet transfusions were considered to be appropriate, 38% (869/2283) outside of guidelines, and in 6% (153/2283) there was insufficient information to determine appropriateness.[5] However, this algorithm was felt to be unnecessarily restrictive because it did not allow for other reasons that seemed to be equally valid but that were not specifically mentioned within the BCSH guidelines.

An updated algorithm (Appendix 1) was therefore devised, and according to this algorithm 60% were considered to be appropriate, 34% outside of guidelines, and in 6% there was insufficient information to determine appropriateness. See table below.

Results of prophylactic transfusion algorithm	National		Your site (15 cases)	
	Number	%	**Number**	**%**
Acceptable platelet transfusion	1375/2283	60	**11**	**73**
Outside platelet transfusion guidelines	782/2283	34	**3**	**20**
Indeterminate: Platelet transfusion cannot be assessed as appropriate	126/2283	6	**1**	**7**

Overall the algorithm was generous and allowed all stated reasons for an increased threshold to be accepted. Patients with MDS (242 cases) were classified as outside of guidelines.

Although some patients with MDS have a legitimate reason for prophylactic platelet transfusion this is not easily assessed in an algorithm based on the timing of the count or the use of a threshold to define appropriateness. Further analysis of the reasons for transfusion within this group estimate that, at most, only 22% (53/242) of cases had valid reasons for transfusion. These reasons included: previous significant haemorrhage (13); fever (14); systemic infection (15); therapeutic anticoagulation (1); therapeutic antifungals (1); and other (16).

[5] Of those that were considered appropriate 6% (75/1281) were only classified as such because the patient had a fever.

Appropriate transfusions were higher in paediatric compared to adult cases at 74% (112/151) and 59% (1263/2132) respectively. Predictably, inpatient cases were more likely to be appropriate at 67% (961/1432) compared to outpatient cases at 49% (414/851).

The most common reasons for classification outside of guidelines were transfusion above a threshold count (28%, 602/2132) and transfusion to patients with MDS (9%, 189/2132) without a reason for either documented in the notes.

BLEEDING POST PLATELET TRANSFUSION

23 patients (1%) had significant bleeding in the 24 hours following the platelet transfusion. In 4/23 the bleeding caused haemodynamic compromise as defined by a drop in systolic or diastolic BP of > 30mmHg. In 15/23 extra blood products were required - 9 patients required two or more units of RBCs, 11 required platelets (4 required two or more units), 2 required FFP and 1 required cryoprecipitate. No other interventions were reported to be necessary to stop the bleeding.

PRE-PROCEDURE PLATELET TRANSFUSIONS

15% (497/3296) of all cases received platelets pre-procedure. **Your site: 2 case(s)**

TYPE OF PROCEDURE

497 cases had 536 procedures. The most common procedure for which a pre-platelet transfusion was given was line insertion (28%) followed by surgery not involving the eye or brain (23%). 12% of all procedures were bone marrow examinations.

Procedures documented	National (536 procedures)		Your site
	Number	%	Number
Bone marrow aspirate and/or trephine	67	12	**0**
Indwelling line insertion (e.g. Hickman line, PICC line, Non-tunnelled central line, Subclavian line, Internal Jugular line, Femoral line, Portacath)	152	28	**1**
Endoscopy only (e.g. OGD/Gastroscopy, Colonoscopy, Bronchoscopy [including Bronchoalveolar lavage], Cystoscopy, etc.)	23	4	**0**
Endoscopy and biopsy	12	2	**0**
Lumbar puncture	51	10	**0**
Epidural anaesthetic	4	0.7	**0**
Organ biopsy (e.g. liver biopsy, open lung biopsy, splenic biopsy)	21	4	**0**
Surgical procedure not involving the eye or brain	122	23	**1**
Surgery/biopsy on eye or brain	6	1	**0**
Don't know	3	0.6	**0**
Other*	75	14	**1**

*Other category included: line removal (35), aspiration (11), drain insertion (8), interventional radiology (6), apheresis/filtration (5), skin biopsy (3), vaginal delivery (3), catheter insertion (2), injection (1).

TIMING OF PLATELET TRANSFUSION

In only 81% of cases was the transfusion given within the 6 hours prior to the procedure. See table below.

Was the platelet transfusion given in the 6 hours that immediately preceded the procedure?	**National (497 cases)**		**Your site (2 cases)**	
	Number	**%**	**Number**	**%**
Yes	402	81	**2**	**100**
No	84	17	**0**	**0**
Not known	11	2	**0**	**0**

STANDARD 3

3a.

The threshold for prophylactic platelet transfusions should be 50 x 10^9/L prior to invasive procedures (gastroscopy and biopsy, liver biopsy, laparotomy, etc.) if the patient has no other risk factors for haemorrhage.

In a significant number of procedures the pre-transfusion platelet count was above 50 x 10^9/L. This was most common prior to surgical procedures not involving the eye or brain where 29% (32/109) of all procedures received a platelet transfusion at counts above this level. Although epidural anaesthesia was uncommon within this audit (4 cases), the proportion that were transfused above the threshold of 50 x 10^9/L was high (50%). See table below.

Procedures performed within a threshold of 50 x 10^9/L	National		Your site
	Number ≤50	% ≤50	Number
Indwelling line insertion (e.g. Hickman line, PICC line, Non-tunnelled central line, Subclavian line, Internal Jugular line, Femoral line, Portacath)	123/149	83	/
Endoscopy only (e.g. OGD/Gastroscopy, Colonoscopy, Bronchoscopy [including Bronchoalveolar lavage], Cystoscopy, etc.)	18/22	82	/
Endoscopy and biopsy	7/12	58	/
Lumbar puncture	40/51	78	/
Epidural anaesthetic	2/4	50	/
Organ biopsy (e.g. liver biopsy, open lung biopsy, splenic biopsy)	12/20	60	/
Surgical procedure not involving the eye or brain	77/109	71	1/ 1
Don't know	2/2	100	/
Other	65/70	93	/

3b.

The threshold for prophylactic platelet transfusions should be 100 x 10^9/L prior to operations in critical sites such as the brain or eyes.

Only 6 cases had procedures involving the eye or brain and in all the pre-procedure platelet count was below 100 x 10^9/L.

3c.

The threshold for prophylactic platelet transfusions should be 40 x 10^9/L prior to lumbar puncture or central line insertion in paediatric patients.

71% (27/38) of paediatric cases had a platelet count ≤ 40 x 10^9/L See table below

Paediatric patient procedures performed within a threshold of 40 x 10^9/L	**National**		**Your site**
	Number ≤40	**%** ≤40	**Number**
Lumbar puncture OR Indwelling line insertion (+/- bone marrow examination but excluding other procedures)	27/38	71	**/**

STANDARD 5

A platelet transfusion is not necessary prior to a bone marrow biopsy.

In 9% of cases (45/497) where the only procedure performed was a bone marrow aspirate and/or trephine biopsy platelets were given. See table below.

Procedure	National		Your site (2 cases)	
	Number With Tx	%	Number	%
Bone marrow aspirate and/or trephine ALONE	45/497	9	**0**	**0**

Reason for transfusion outside of guidelines

30% (48/160) of all those reported as outside guidelines gave a total of 53 reasons for why the transfusion was given. In only 11 of these was an individual threshold stated in the notes.

STANDARD 4

The post-transfusion platelet count should be checked prior to the procedure to ensure there has been a response to the platelet transfusion.

Despite BCSH guidelines, in only 30% of cases was a platelet count checked pre-procedure. See table below.

Platelet count checked post transfusion and pre-procedure	National (497 cases)		Your site (2 cases)	
	Number	%	Number	%
Yes	151	30	**0**	**0**
No	333	67	**2**	**100**
Not known	13	3	**0**	**0**

Reason why platelet count was not performed

In the majority of cases there was no obvious reason for the omission. See table below.

If no pre-procedure count was it because the patient died or was transferred out of the hospital before a count was done?	National (333 cases)		Your site (2 cases)	
	Number	%	Number	%
Yes	33	10	**2**	**100**
No	274	82	**0**	**0**
Not known	26	8	**0**	**0**

ALGORITHM

To further evaluate the appropriateness of transfusion in both adult and paediatric cases a pre-procedure platelet transfusion algorithm was devised which considered the pre-transfusion platelet count, the timing of the count, the diagnosis, BCSH guidelines which recommend a threshold platelet count or the presence of an individual safe platelet threshold documented in the notes(Appendix 1).

Similar to the prophylactic algorithm, the pre-procedure algorithm was designed to be generous. This allowed patients with MDS or a platelet function defect not to have had a recent count and did not include the need for the transfusion to have occurred within 6 hours of the procedure or a post transfusion count to be checked prior to the procedure. A platelet count of 50 x 10^9/L prior to lumbar puncture or central line insertion was used for both adult and paediatric patients as it was clear that the BCSH paediatric threshold of 40 x 10^9/L was not applied in most sites.

Using this algorithm 64% of all platelet transfusions were considered to be appropriate, 23% outside of guidelines and in 13% there was insufficient information to determine appropriateness.

Results of pre-procedure transfusion algorithm	National		Your site	
	Number	%	Number	%
Acceptable platelet transfusion	319/497	64	**1**	**50**
Outside platelet transfusion guidelines	114/497	23	**0**	**0**
Indeterminate: Platelet transfusion cannot be assessed as appropriate	64/497	13	**1**	**50**

Appropriate transfusions were higher in paediatric than adult cases at 76 % (41/54) and 63% (278/443) respectively. The number of appropriate transfusions was similar in inpatients and out-patients at 65% (251/387) and 62% (68/110) respectively.

The most common reasons for classification outside of guidelines were transfusion when the only procedure performed was a bone marrow aspirate and/or trephine biopsy (9%, 45/497) and transfusion above a defined threshold of 50 x 10^9/L prior to surgical procedures excluding eyes and brain (6%, 32/497).

If strict application of BCSH guidelines and a threshold of 40 x 10^9/L had been applied to all paediatric cases who had either a lumbar puncture or central line inserted, < 1% (4/497) of transfusions would have been re-categorised as outside platelet transfusion guidelines.

EXCESSIVE BLEEDING POST PROCEDURE

23 patients (5%) were reported to have excessive bleeding in the 24 hours following the procedure.

61% (14/23) of these had surgical procedures and accounted for:-

- 75% of cases with haemodynamic compromise
- 70% of cases needing extra red cell and/or platelet support
- All cases who required additional surgery

6 of these 14 surgical cases had a diagnosis of ITP.

Overall in 4/23 cases the bleeding caused haemodynamic compromise as defined by a drop in systolic or diastolic BP of > 30mmHg.

In 20/23 cases extra blood products were required - 12 required two or more units of RBC, 14 required platelets (6 required two or more units) 2 required FFP and 1 required cryoprecipitate. 8 cases needed other interventions to stop the bleeding (3 anti-fibrinolytics, 3 surgery, and in 4 either cautery or pressure was applied).

THERAPEUTIC PLATELET TRANSFUSIONS

13% (412/3296) of all cases received platelets to treat bleeding. **Your site: 3 case(s).**

The most common categories were nose bleeds, malaena and large or multiple bruises.
599 different categories of haemorrhage were reported in these 412 cases. See table below.

Site of haemorrhage	Type of haemorrhage	Severity of haemorrhage	Number	% of 599	Your site
Skin	Petechiae	Rash localised to 1-2 sites/ sparse *	24	4	0
		Rash spreading/confluent/ more than 2 areas of body	33	6	1
	Bruises	1-2 small bruises 2-10cm in size*	31	5	0
		Large (>10 cm)/multiple (> 2cm)/ or spreading	45	8	2
Mouth and/or throat	Blood blisters	Asymptomatic*	14	2	0
		Bleeding/symptomatic	31	5	0
		Bleeding lasting < 30 minutes*	12	2	0
		Bleeding lasting ≥ 30 minutes	23	4	0
Nosebleed		Bleeding lasting < 30 minutes*	46	8	0
		Bleeding lasting ≥ 30 minutes	65	11	0
Haemoptysis			20	3	0
GI bleeding	Haematemesis		30	5	0
	Visible blood in stool		33	6	1
	Malaena		52	9	0
GU bleeding	Visible haematuria		33	6	0
	Abnormal vaginal bleeding (more than spotting of blood)		22	4	0
Blood in body cavity fluids (e.g. pleural tap, ascitic tap)			5	1	0
Retinal haemorrhage		Without visual impairment	5	1	0
		With visual impairment	3	0.5	0
Intra-cranial haemorrhage		Without neurological signs	3	0.5	0
		With neurological signs	15	3	0
Abnormal bleeding at site of previous procedure			27	5	0
Bleeding but site and/or severity not documented in the notes			27	5	0

In 18% (73/412) of cases the bleeding caused haemodynamic compromise (defined as a drop in systolic or diastolic BP of > 30mmHg) and in 21% (87/412) additional blood products were required prior to the audited transfusion.

BLEEDING POST PLATELET TRANSFUSION

In 58% (239/412) of cases bleeding stopped following the audited transfusion but in 39% (159/412) bleeding continued. In those that continued bleeding 70% (112/159) required extra blood products (See table below) and 43% (68/159) required other interventions.

Extra blood products

Blood Product	Number of Cases	Median	IQR	Range
RBCs	85	3	2 to 4	1 to 26
Platelets	73	2	1 to 3	1 to 39
FFP	29	4	2 to 7	2 to 13
Cryoprecipitate	19	2	1 to 2	1 to 9

Interventions included anti-fibrinolytics (18), endoscopy (15), surgery (14), other drugs to stop bleeding e.g. omeprazole, norethisterone, DDAVP, protamine, vitamin K, heparin stopped (10), pack/cautery/variceal banding/compression bandage/embolisation (7), steroids/IVIG (3), Beriplex (2), factor VIIa (2), fibrin glue or other topical haemostatic agents (1).

STANDARD 6

Patients with immune thrombocytopenia or thrombotic thrombocytopenic purpura should only receive platelet transfusions if there is life-threatening bleeding.

30 patients who received therapeutic platelet transfusions had a diagnosis of ITP. 11 were WHO grade 4 bleeding (life-threatening) and considered appropriate. In the remaining 19, 3 had grade one bleeding and all were classified as outside of guidelines. See table below.

Number of ITP/TTP cases with life-threatening bleeding	National		Your site Number
	Number	%	
ITP or TTP	11/30	37	**0/ 1**

ALGORITHM

To further evaluate bleeding and the appropriateness of transfusion in both adult and paediatric cases a therapeutic platelet transfusion algorithm was devised which considered the severity of bleeding, as classified by the World Health Organisation (WHO) and the diagnosis. Bleeding of WHO grade 1 is not clearly covered by BCSH guidelines and therefore considered an indeterminate indication. All cases of ITP or TTP outside of life threatening bleeding were considered outside of guidelines (BCSH guidelines) and all other types of bleeding were considered appropriate. See appendix 1.

84% (345/412) were considered acceptable, 12% (48/412) indeterminate and 5% (19/412) outside of platelet guidelines. Of the 48 indeterminate cases, 38 had WHO grade 1 bleeding and 10 had insufficient information to allow further assessment. All 19 cases that were classified as outside of guidelines had ITP with non-life-threatening bleeding. 3/19 of these cases had WHO grade 1 bleeding. See tables below.

Results of therapeutic transfusion algorithm	National		Your site (3 cases)	
	Number	%	Number	%
Acceptable platelet transfusion	345/412	84	**2**	**67**
Outside platelet transfusion guidelines	19/412	5	**1**	**33**
Indeterminate: Platelet transfusion cannot be assessed as appropriate	48/412	12	**0**	**0**

WHO grade of bleeding	National		Your site (3 cases)	
	Number	%	Number	%
Grade 1	41/412	10	**0**	**0**
Grade 2	220/412	53	**2**	**67**
Grade 3	38/412	9	**0**	**0**
Grade 4	87/412	21	**0**	**0**
Unclassified by algorithm	26/412	6	**1**	**33**

REASON FOR PLATELET TRANSFUSION UNKNOWN

In 104 cases the auditor was unable to determine the reason why the platelet transfusion was given. See table below.

	National (3296 cases)		Your site (20 cases)	
	Number	%	Number	%
Reason for transfusion not clear from patient records	104	3.2	0	0

BLEEDING POST PLATELET TRANSFUSION

2 patients (2%) had significant bleeding in the 24 hours following the platelet transfusion. In 1 of the 2 the bleeding caused haemodynamic compromise as defined by a drop in systolic or diastolic BP of > 30mmHg and this patient required extra blood products (4 units RBC, 2 units platelets, no FFP, no cryoprecipitate). The other patient required no extra blood product but was given anti-fibrinolytics.

INFORMATION ABOUT PLATELETS TRANSFUSED

76% (2517/3296) had further platelet transfusions during the audit 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 to 11 and range 1 to 101 (including the audited transfusion episode).

To obtain an impression of what percentage of platelet units were used by the audited cases, platelet issue data for the 3 month period for all participating sites was obtained from the Blood Stocks Management Scheme (BSMS) and totalled 36,331 units. To give a conservative estimate of percentage used by the audited cases only one unit was presumed to have been transfused at additional transfusion episodes and this was added to the number of units transfused in the audited episode. This gave a total of 16,703 units which represents 46% (16,703/36,331) of all units issued to these sites over the audit period.

3288 cases out of 3296 (3060 adults and 228 paediatric), provided either the number of adult units transfused or if $\leq$ 20kg the volume transfused in mls. 1 case received 4 paedipacks and for 7 no data were provided.

DATA FOR ADULT CASES

85% (2607/3060) received one unit, 13% (408/3060) received two units, 1% (30/3060) received three units and 0.5% (15/3060 cases) received more than 3 units (range 4 to 110).

DATA FOR PAEDIATRIC CASES

Paediatric cases received both adult units and volume in mls. In 91 cases doses were stated in mls and in 66 of these the patient weighed under 20 kg. For those weighing under 20 kg the median dose was 150ml, IQR 90-200ml and range 40-250 ml (median dose/kg 13.6ml, IQR 14 to 14.7ml and range 5 to 20ml).

EXPIRY OF PLATELETS

In 23% of cases (764/3296) at least one unit was due to expire at midnight on the day of transfusion. In 76% (2518/3296) of cases none of the units expired that day and in 14 cases this information was unknown.

COMPLICATIONS OF PLATELET TRANSFUSIONS

4% (120/3296) of all cases suffered an adverse event within 24 hours of the platelet transfusion. In 6 cases this information was unknown.

In 35% (42/120) this was considered to be a transfusion reaction. 6 cases were reported as febrile reactions with other symptoms/signs, 3 cases were isolated febrile reactions, 32 cases were allergic (30 minor but 2 severe) and 1 case developed hypotension.

In 57 cases the adverse event was not considered transfusion related. 14 patients died and in 43 additional cases the problem was: fever, sepsis, or infection related (29); bleeding (4); deterioration (3); rash (4); pain (1); vomiting (1); or ATRA syndrome (1). In 4 cases the problem was unknown.

DISCUSSION

A large proportion of all eligible hospitals within the UK participated in this audit. The results are therefore likely to provide an accurate reflection of current practice in this patient population. Also, 46%[6] of all platelets issued to participating sites during September to November 2010 were used by the audited cases. This is in keeping with previous recent estimates of total platelet usage by haematology patients [13, 14] & [Appendix 2]. This audit therefore represents a large proportion of all platelets used and has the potential to identify ways in which demand for platelets could be reduced, as well as predicting future platelet needs.

ORGANISATIONAL SURVEY

Two standards were defined for the organisational audit, these related to the availability of written local guidelines and the implementation of local audit to assess compliance. It is reasonable to expect all sites to have written guidelines, and 96% (118/123) of sites complied with this standard. In contrast, only 50% (61/123) stated that local audits were performed and in only 43% (26/61) of these had this occurred in the last 12 months. This probably reflects the fact that a requirement for regular audit is difficult to achieve because it is labour intensive, requiring hand-searching of notes. Clear documentation of transfusion indications within patients' notes would make this process easier, in the short term, but information technology solutions are required. The Clinical Tracking of Blood Project, managed by the BSMS/NHSBT, aims to link the reason for transfusion with laboratory parameters and therefore has the potential to achieve this objective. Five pilot sites have been identified to progress this and a feasibility report is expected in March 2012.

Most sites, 82% (101/123), had common guidelines for platelet transfusion in adult and paediatric patients. In keeping with BCSH guidelines for the use of platelets[3], 98% (117/119) of sites with adult or combined guidelines stated that a threshold of 10 x 10^9/L would be used for stable patients with reversible bone marrow failure. Most sites increased this threshold for conditions considered to increase the risk of bleeding, but there was disagreement regarding which situations these were and the revised threshold which should be used. This is likely to be due, in part, to the subsequent publication of disease or population specific guidelines [5-9, 15] that recommended different transfusion thresholds to the original guidelines [3]. As a consequence, patients with the same condition or situation managed at different sites are transfused at different counts.

An additional cause for differences in transfusion practice between sites is likely to be because of the variety of definitions used for fever and infection. For example, 10% (10/96) of sites that defined fever changed their transfusion threshold for temperatures of 37.5^{o}C or above and 1 site changed its transfusion threshold if a patient had a sustained temperature above 37^{o}C.

[6] Using a conservative estimate

Although there is confusion over risk factors and threshold platelet counts to guide prophylactic platelet transfusion there should be none regarding the unnecessary use of platelets for patients with long term bone marrow failure or prior to performing a bone marrow aspirate or bone marrow aspirate and trephine. Despite this 36%, 12% and 23% respectively of adult or combined adult and paediatric guideline sites indicated that these would be given routinely below a threshold count.

Of note, the recommended threshold of 20 or 40 x 10^9/L prior to line insertion or lumbar puncture for paediatric patients has not been widely adopted. This threshold was not used in any paediatric only guidelines for insertion of indwelling lines and at only 3 sites out of 34 for lumbar puncture.

Short term reinforcement of currently agreed guidance regarding when platelet transfusions are required is needed. Longer term revised national guidelines are required, based on evidence from systematic reviews, once on-going randomised controlled trials of prophylactic platelet transfusion have been completed.

CLINICAL AUDIT

60% of all audited cases were aged 60 years or over and the most common underlying haematological diagnoses (AML, lymphoma, myelodysplasia) are more common in older age groups. Therefore, given the increasing age of the population, the use of platelet transfusions will continue to increase if no change to current practice occurs.

Seven standards were defined in the clinical section of the audit.
There were two general standards:

- Need for a recent pre-transfusion platelet count
- Documentation of the reason for transfusion in the patient's notes

8% (250/3296) of cases did not have a platelet count within 24 hours if an inpatient or 48 hours if an outpatient. Out-patient cases were less likely to comply and represented 62% (155/250) of all non-compliant cases. Only 18% (44/250) had a diagnosis of MDS, in which the platelet count would not be expected to change. There is therefore likely to be significant room for improved practice in the remainder.

Similarly, although auditors were able to identify the reason for transfusion in 97% of cases, this was only clearly documented in the notes of 72% of cases, suggesting improved documentation is required.

Five standards were more specific and 3 of these were used in the appropriate use algorithms.

Two pre-procedure standards, not included in the appropriate use algorithms, looked at the timing of the transfusion and the need for a post-transfusion platelet count prior to the

procedure. In only 81% was the transfusion given within 6 hours of the procedure and in only 30% was the platelet count checked before the procedure. Improved compliance would be expected to maximise and verify effectiveness.

Given the criticism of the previous audit for not taking into account factors which may alter the individual threshold for each patient, lenient algorithms to assess appropriateness were devised for prophylactic, pre-procedure and therapeutic transfusions. Appropriate use was considered to have occurred in 60% of prophylactic, 64% of pre-procedure and 84% of therapeutic use. Using outside of guideline data for prophylactic and pre-procedure algorithms an estimated 896 transfusion episodes could potentially have been avoided which represents 27% of all transfusions given.

The main reasons that platelet transfusions were classified as outside of guidelines were:

- Prophylactic transfusions – transfusion above a threshold count (28%, 602/2132) and transfusion to patients with MDS (9%, 189/2132) without a reason for either documented in the notes.
- Pre-procedure - transfusion when the only procedure performed was a bone marrow aspirate and/or trephine biopsy (9%, 45/497) and transfusion above a defined threshold of 50 x 10^9/L prior to surgical procedures excluding eyes and brain (6%, 32/497).

Considerable improvement in practice and reduced use would therefore seem possible.

Additional information collected in this audit identified the dilemma sites face in deciding whether units of platelets should be routinely stocked or ordered as required. In 64% of all sites blue light delivery time was greater than one hour. On site availability would allow transfusion according to guidelines but increase wastage through time expiry. In this audit platelet wastage (5.8%) was double that of red cells (2.3%) and 23% of all cases (764/3296) were given at least one unit which was due to expire at midnight on the day of transfusion.

In summary, this was a large audit 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.

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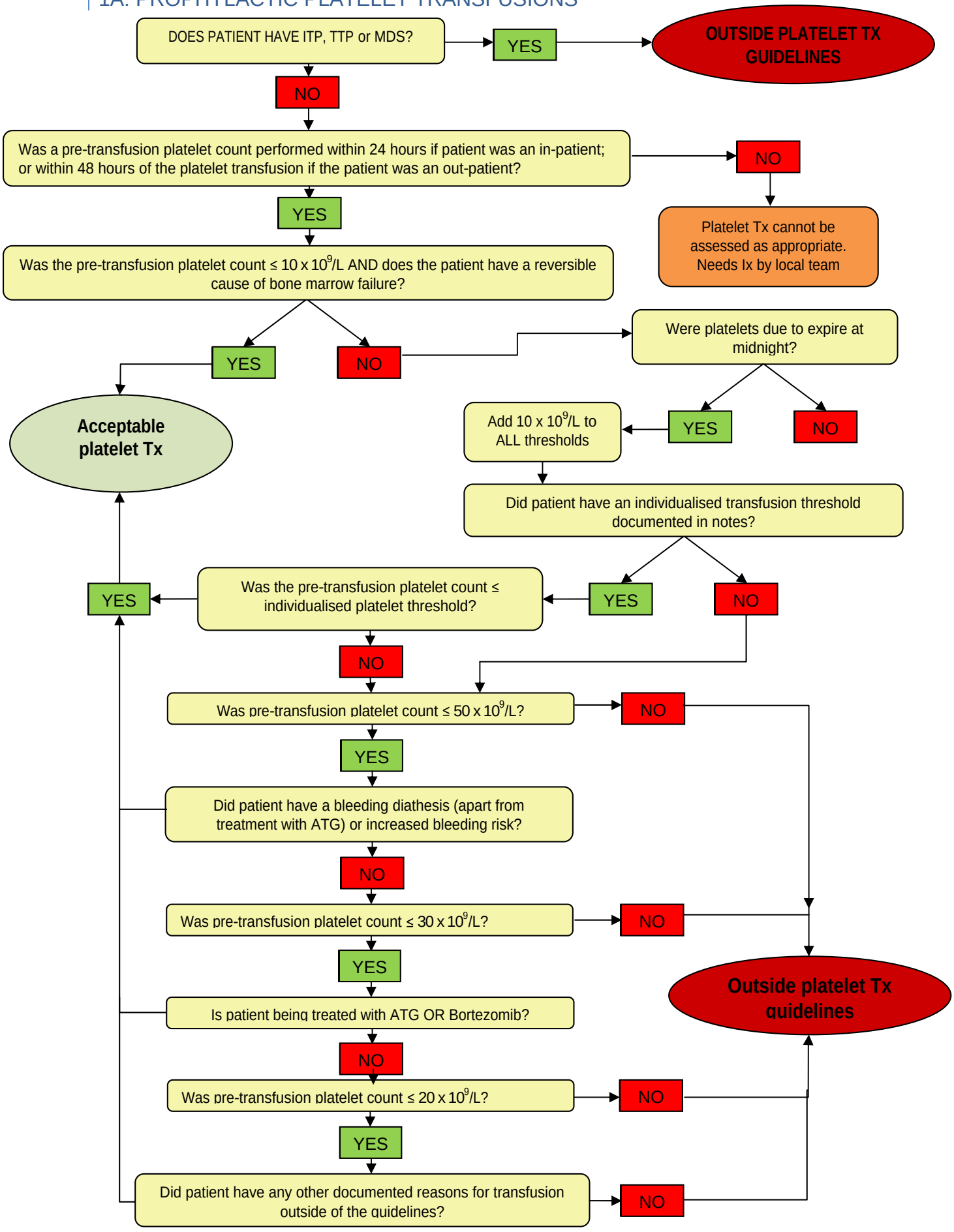
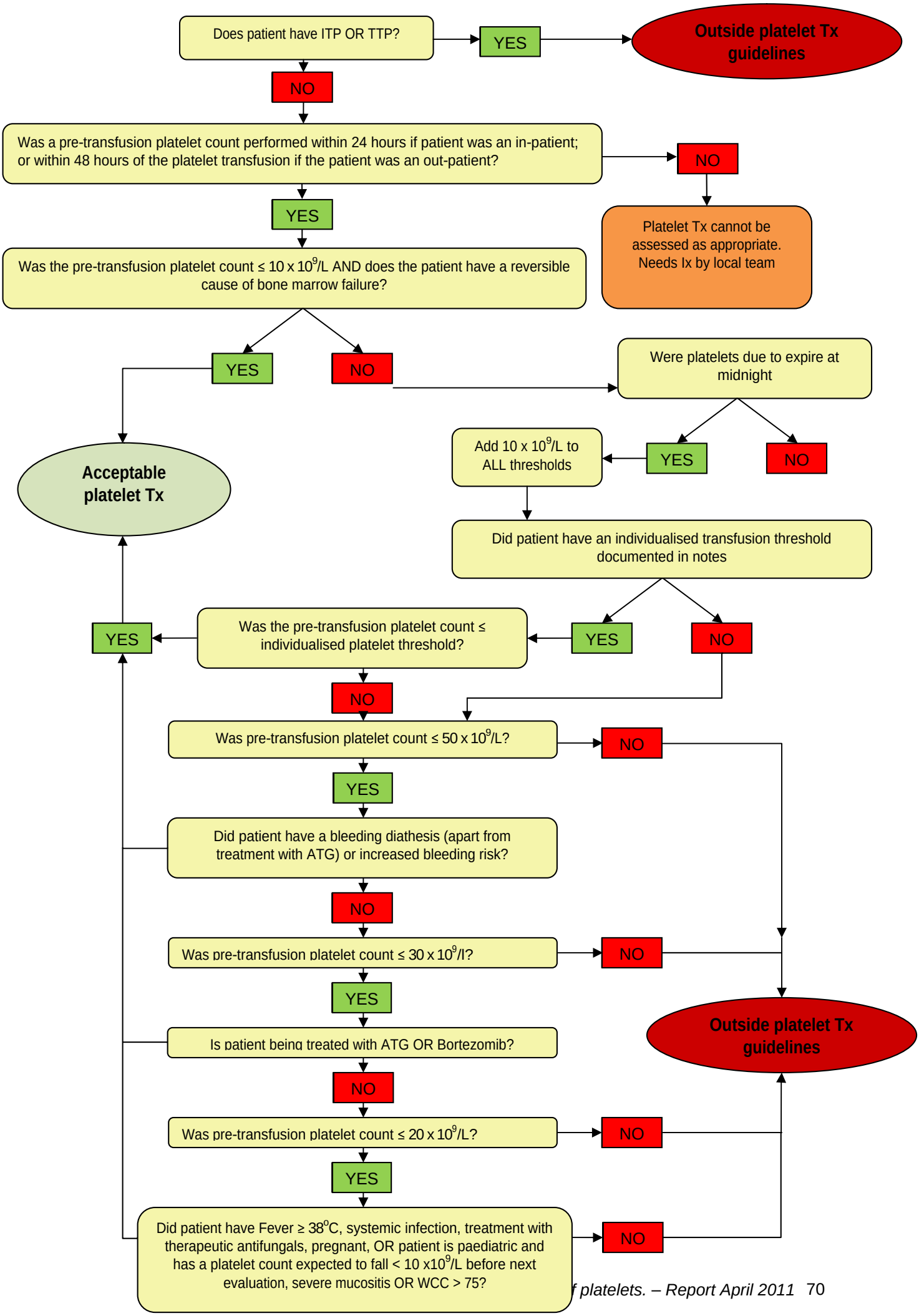
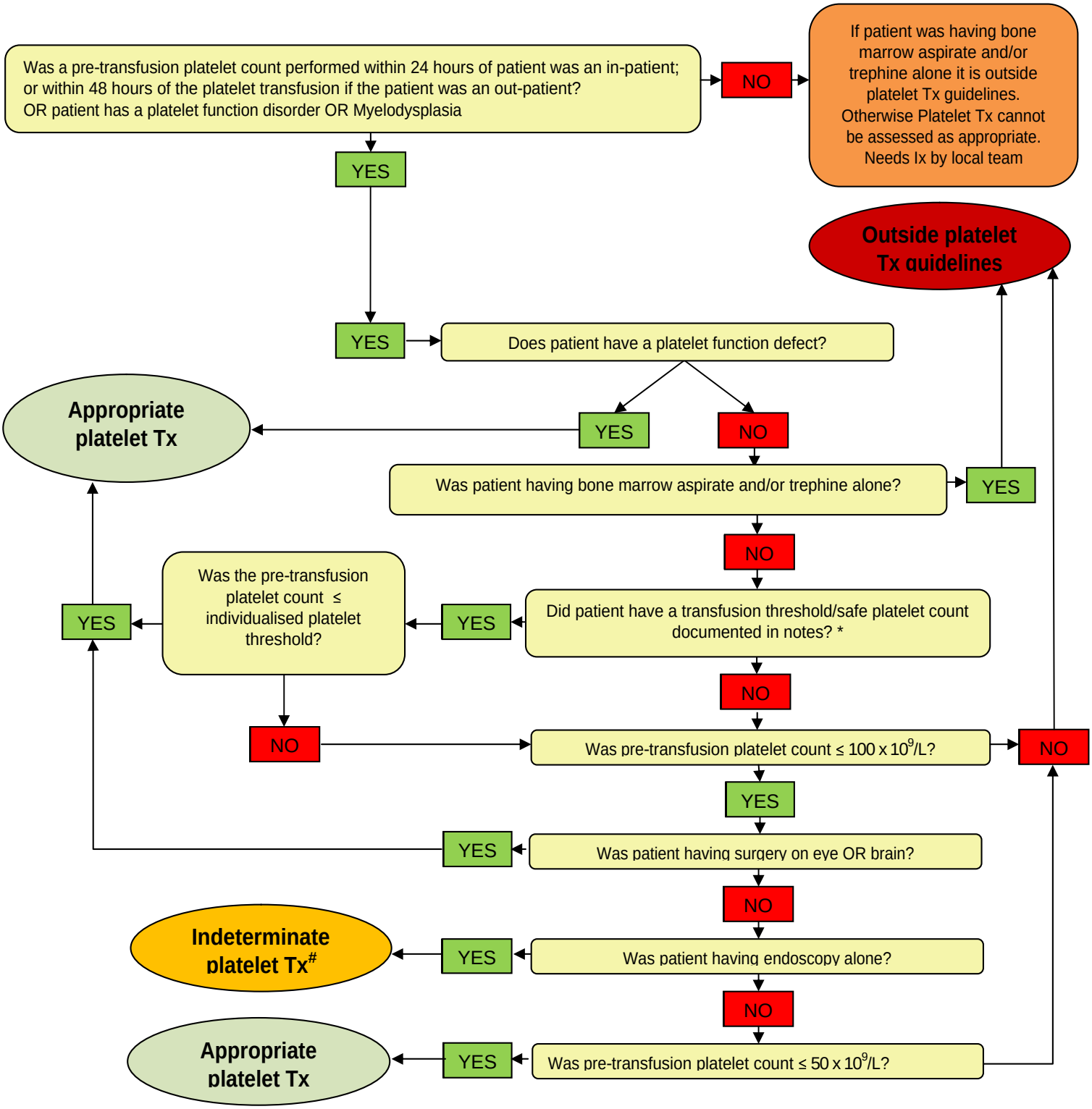
APPENDIX 1: ANALYSIS ALGORITHMS

1A: PROPHYLACTIC PLATELET TRANSFUSIONS




Does patient have ITP OR TTP?
YES
Outside platelet Tx guidelines
NO
Was a pre-transfusion platelet count performed within 24 hours if patient was an in-patient; or within 48 hours of the platelet transfusion if the patient was an out-patient?
NO
Platelet Tx cannot be assessed as appropriate. Needs Ix by local team
YES
Was the pre-transfusion platelet count ≤ 10 x 10^9/L AND does the patient have a reversible cause of bone marrow failure?
YES
NO
Were platelets due to expire at midnight
YES
NO
Add 10 x 10^9/L to ALL thresholds
Acceptable platelet Tx
Did patient have an individualised transfusion threshold documented in notes
YES
Was the pre-transfusion platelet count ≤ individualised platelet threshold?
YES
NO
NO
Was pre-transfusion platelet count ≤ 50 x 10^9/L?
NO
YES
Did patient have a bleeding diathesis (apart from treatment with ATG) or increased bleeding risk?
NO
Was pre-transfusion platelet count ≤ 30 x 10^9/l?
NO
YES
Outside platelet Tx guidelines
Is patient being treated with ATG OR Bortezomib?
NO
Was pre-transfusion platelet count ≤ 20 x 10^9/L?
NO
YES
Did patient have Fever ≥ 38°C, systemic infection, treatment with therapeutic antifungals, pregnant, OR patient is paediatric and has a platelet count expected to fall < 10 x10^9/L before next evaluation, severe mucositis OR WCC > 75?
NO

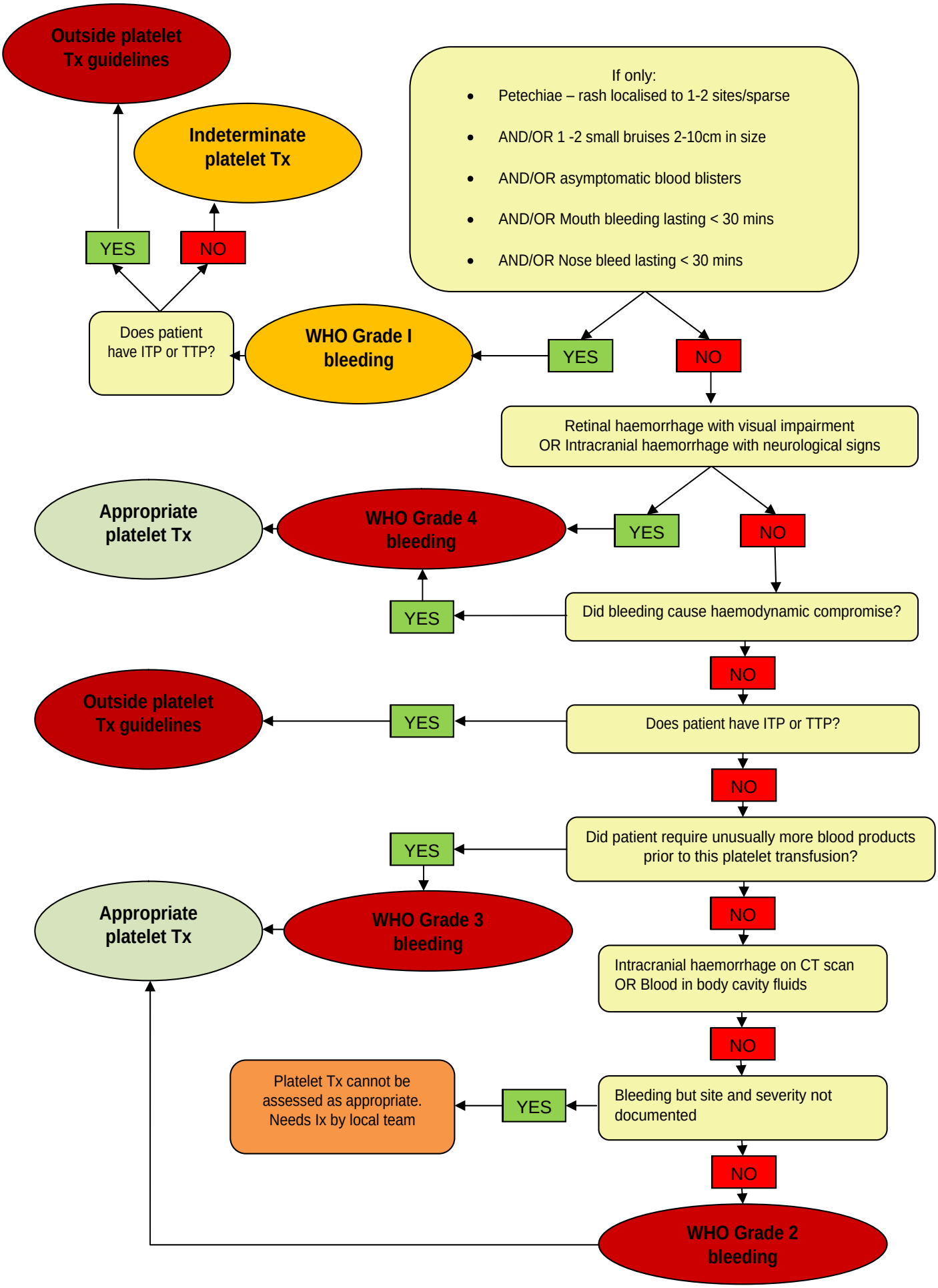
1B: PRE-PROCEDURE PLATELET TRANSFUSIONS



*Essential for a platelet transfusion threshold/ safe platelet count to be documented in the notes if it differs from the general guidelines. This allows adequate communication between haematologists, surgeons, anaesthetists and radiologists. Q. 45 gives reason why transfusion threshold was altered.

No threshold guidance within BCSH guidelines. Threshold of 50 x 10^9/L for endoscopy plus biopsy.

1C: THERAPEUTIC PLATELET TRANSFUSIONS: SEVERITY OF BLEEDING



APPENDIX 2: DATA FROM NW PLATELET USAGE AUDIT PENDRY ET AL 2010

METHODS

All NHS and Independent Hospitals/ Trusts in North West England and North Wales were invited to participate in the audit in February 2010. The audit consisted of two parts: an organisational survey and a single page proforma to be completed on each transfusion episode occurring during the month of March 2010 using data available in the hospital transfusion laboratory without the need to review the patient's case notes.

AUDIT SAMPLE

32 of 34 NHS Hospitals / Trusts in the North West of England and North Wales participated (94%). In addition, 3 independent hospitals were invited but none took part. Audit proformas were completed on 1550 platelet transfusion episodes, accounting for 1911 doses of platelets. During the period, 2613 platelet doses were issued to these hospitals by NHSBT. Data collection has therefore captured 73% (1911/2613) of platelets issued in March 2010.

RESULTS

Clinical usage patterns

By a large margin, Haematology was the commonest clinical specialty for platelet usage, accounting for 57% (890/1550) episodes. Of the other specialties there was a fairly even spread, with the next five largest specialties being: ITU 7.9% (122 episodes), cardiac surgery 6.5% (101), oncology 6.3% (98), general medicine 5.4% (83) and general surgery 3.7% (58). There was very little platelet use in Accident and Emergency (A+E), orthopaedics and trauma and obstetrics. 64% of the transfusion episodes were for prophylaxis, 22% for bleeding and in 14% the information was not given.

When looking at the age demographic, 100 episodes occurred in the neonatal period (6.5%) and another 110 (7.1%) in children and young adults from 1 – 19 years. As in other studies [2,3], platelet use increased significantly with age, with 70 to 79 year olds accounting for 400 episodes (25.8%).

Wastage as percentage of issue ranged from 0% to 27%. 50% had wastage of more than 5%. There was a tendency for those who kept stock platelets to have increased wastage. All Trusts except one participate in the Blood Stocks Management scheme (BSMS).

APPENDIX 3: BCSH GUIDELINES

PROPHYLACTIC PLATELET TRANSFUSIONS

	Platelet Transfusion Threshold							
	No platelet Tx	10	20	30	40	100	Higher threshold (not specified further)	No recommendations
Stable patient with reversible cause of bone marrow failure		•						
Acute promyelocytic leukaemia			•					
Chronic stable thrombocytopenia	•							
Specific treatments								
Stem cell transplantation		•						
Treatment with ATG				•				
Treatment with Bortezomib				•				
Infection/Sepsis/Fever								
Fever			•					
Infection/Sepsis							•	
Treatment with antibiotics							•	
Treatment with antifungals								•
Haemostatic abnormalities								
Abnormalities of haemostasis							•	
DIC (not bleeding)/Chronic DIC		•						
DIC (paediatrics)			•					
DIC + induction treatment for acute leukaemia (paediatrics)					•			
Anticoagulant therapy			•					
Antiplatelet therapy								•
Other factors pre-disposing to bleeding								
Previous significant bleed			•					
Severe hyperleucocytosis					•			
Severe mucositis			•					
Local tumour infiltration			•					
Other reasons within guidelines								
Platelet count likely to fall to < 10 x10^9/l before next evaluation			•					
Pregnancy			•					
Neonates								
Stable preterm or term neonate (not bleeding)			•					
Sick preterm or term infant (not bleeding)				•				
Low birth weight neonate							•	
Neonatal alloimmune thrombocytopenia				•				
ECMO						•		

Stable patients with reversible cause of bone marrow failure

BCSH Guidelines [3, 5-7] recommend a platelet count threshold of 10 x 10^9/L if the patient is stable. *"Platelet transfusions are given to support thrombocytopenia with a transfusion threshold of 10 x 10^9/L unless there are additional risk factors."*

Acute Promyelocytic Leukaemia (APL)

BCSH Guidelines for platelet transfusions [3] recommends *"As a minimum, the platelet count should be kept above 20 x 10^9/L in patients who are haemorrhagic."*

Chronic stable thrombocytopenia e.g. myelodysplasia

BCSH Guidelines for platelet transfusions [3] recommend *"A specific threshold for transfusion may not be appropriate for patients with chronic stable thrombocytopenia who are best managed on an individual basis depending on the degree of haemorrhage"*

Stem cell transplantation

BCSH Guidelines for platelet transfusions [3] do not recommend a change in the transfusion threshold for patients receiving a stem cell transplant.

Patient is receiving Anti-thymocyte globulin (ATG)

BCSH Guidelines for aplastic anaemia [6] recommends *"Platelet transfusions should be given to maintain a safe platelet count (ideally >30 x 10^9/L), but should not be given concurrently with ATG administration because of the anti-platelet activity of ATG.*

Patient is receiving Bortezomib (Velcade)

BCSH guidelines on the diagnosis and treatment of multiple myeloma [15] state that *"Thrombocytopenia: usually progressive over 21-day cycle with recovery prior to next cycle. Check FBC on days 1 and 8"*

"The platelet count should be >30 x 10^9/L to treat and patients may receive platelet transfusions to allow this. If platelet count is <30 x 10^9/L on day 1, dose reduction should be considered e.g. to 1mg/m^2. Thrombocytopenia tends to become less severe with time on treatment."

Fever

BCSH Guidelines for management of aplastic anaemia [6] recommends *"Prophylactic platelet transfusions should be given when the platelet count is....<20 x 10^9/L in the presence of fever"*

Infection

BCSH Guidelines [3, 7] recommend higher platelet transfusion threshold if risk factors present. *"Risk factors include sepsis, concurrent use of antibiotics or other abnormalities of haemostasis."*

Therapeutic antibiotics

BCSH Guidelines [3, 7] recommend a higher platelet transfusion threshold if risk factors present. *"Risk factors include sepsis, concurrent use of antibiotics..."*

Therapeutic antifungal drugs

There are no specific recommendations for anti-fungal medications.

Abnormalities of haemostasis

BCSH Guidelines [3, 7] recommend higher platelet transfusion threshold if risk factors present. *"Risk factors include ... abnormalities of haemostasis."*

DIC (Disseminated Intravascular Coagulation)

BCSH Guidelines for neonates and older children [5] recommend platelet transfusions when *"Platelet count <20 x 10^9/L and ....Disseminated intravascular coagulation (DIC)"* OR *"Platelet count 20 to 40 x 10^9/L and...DIC in association with induction therapy for leukaemia"*

BCSH Guidelines for platelet transfusions [3] recommend "In chronic DIC or in absence of bleeding platelet transfusions should not be given merely to correct a low platelet count."

Therapeutic anticoagulant drugs

BCSH Guidelines [3, 7] recommend higher platelet transfusion threshold if risk factors present. "Risk factors include ....abnormalities of haemostasis."

BCSH Guidelines for neonates and older children [5] recommends platelet transfusion if "Platelet count <20 x 10^9/L and .....Anticoagulant therapy"

Therapeutic antiplatelet agents

BCSH Guidelines [3, 7] recommend higher platelet transfusion threshold if risk factors present. "Risk factors include ....abnormalities of haemostasis."

Previous significant bleed

BCSH guidelines on the management of acute myeloid leukaemia in adults [7] states that *"The platelet count should be kept at >20 x 10^9/L in patients who are haemorrhagic."*

Better Blood Transfusion Toolkit recommends a threshold of 20 x 10^9/L where there is a high risk of bleeding e.g. a previously bleeding ulcer.

Mucositis

BCSH Guideline for neonates and older children [5] recommends a platelet transfusion if *"Platelet count <20 x 10^9/L and .....severe mucositis"*

Hyperleucocytosis

BCSH Guidelines for neonates and older children [5] recommends a platelet transfusion when *"Platelet count 20 to 40 x 10^9/L and...severe hyperleucocytosis"*

Local tumour infiltration

BCSH Guideline for neonates and older children [5] recommends a platelet transfusion if *"Platelet count <20 x 10^9/L and .....local tumour infiltration"*

Platelet count is expected to fall to < 10 x 10^9/L before the next evaluation

BCSH Guideline for neonates and older children [5] recommends a platelet transfusion if *"Platelet count <20 x 10^9/L and .....platelet count likely to fall before next evaluation"*

Pregnancy

BCSH Guidelines for aplastic anaemia [6] recommends that *"the platelet count should, if possible, be maintained above 20 x 10^9/L with platelet transfusions."* This is based on the BCSH guidelines for treatment of ITP in pregnancy[8].

Term neonate

BCSH Guidelines for neonates and older children [5] recommends "*Term infants are unlikely to bleed if their platelet count is maintained above 20 x10^9/L"*

Small preterm neonates

BCSH Guidelines for neonates and older children [5] states that a *"higher threshold is generally recommended, particularly during the first few days when the risk of PVH* (peri-ventricular haemorrhage) *is highest or there is evidence of coagulopathy"*

Sick preterm or term neonate (not bleeding)

BCSH Guidelines for neonates and older children [5] states that a threshold of 30 x 10^9/L is generally recommended.

Neonatal alloimmune thrombocytopenia

BCSH Guidelines for neonates and older children [5] states that *"In these patients, a minimum platelet count of 30 x 10^9/L is recommended because the HPA antibody can impair platelet function."*

ECMO

BCSH Guidelines for neonates and older children [5] states that "*Platelet transfusions should be given to maintain the platelet count above 100 x 10^9/L".*

PRE-PROCEDURE PLATELET TRANSFUSIONS

	Platelet Transfusion Threshold						
Procedure	**No platelet Tx**	**20**	**40**	**50**	**80**	**100**	**No recommendations**
Bone marrow aspirate alone	●						
Bone marrow aspirate and trephine	●						
Endoscopy alone							●
Endoscopy plus biopsy				●			
Paediatric lumbar puncture			●				
Adult lumbar puncture				●			
Epidural anaesthetic				●			
Paediatric indwelling line insertion			●				
Adult indwelling line insertion				●			
Organ biopsy				●			
Surgery excluding brain or eye				●			
Surgery of eye or brain						●	

Bone Marrow Aspirate and or trephine

BCSH guideline [3] recommends *"Bone marrow aspiration and biopsy may be performed in patients with severe thrombocytopenia without platelet support, providing that adequate surface pressure is applied"*

Endoscopy without biopsy [7]

No BCSH recommendations

Endoscopy + biopsy

BCSH guideline [3] recommends *"For...gastroscopy and biopsy,.... transbronchial biopsy, ...or similar procedures, the platelet count should be raised to at least 50 x 10^9/L"*

Insertion of an indwelling line

BCSH Guidelines for neonates and older children [5] recommends a platelet transfusion *when "Platelet count 20 to 40 x 10^9/L and...prior to central venous line insertion"*

BCSH guideline for platelet transfusions [3] recommends *"For...insertion of indwelling lines... the platelet count should be raised to at least 50 x 10^9/L"*

[7] The American Red Cross [16. Practice Guidelines for Blood Transfusion. In A Compilation from Recent Peer-Reviewed Literature, Edition American National Red Cross 2007.] recommends that "GI endoscopy without biopsy may be safely performed at platelet counts <20,000/mm^3." AND "Fibre-optic bronchoscopy without biopsy by an experienced operator may be safely performed in the presence of a platelet count <20,000/mm^3."

Lumbar puncture

BCSH Guidelines for neonates and older children [5] recommends platelet transfusion when *"Platelet count 20 to 40 x 10^9/L and...prior to lumbar puncture"*

BCSH guideline for platelet transfusions [3] recommends *"For lumbar puncture... the platelet count should be raised to at least 50 x 10^9/L"*

Epidural anaesthetic

BCSH guideline for platelet transfusions [3] recommends *"For epidural anaesthetic... the platelet count should be raised to at least 50 x 10^9/L"*

Of note the BCSH guidelines for immune thrombocytopenia [8] recommends for *"use of epidural anaesthesia ....the platelet count should be > 80 x 10^9/L."*

Liver biopsy or other organ biopsy

BCSH guideline for platelet transfusions [3] recommends *"For ....liver biopsy ...or similar procedures, the platelet count should be raised to at least 50 x 10^9/L"*

Surgery excluding eye and brain

BCSH guideline for platelet transfusions [3] recommends *"For ....laparotomy ...or similar procedures, the platelet count should be raised to at least 50 x 10^9/L"*

Surgery of eye or brain

BCSH guideline for platelet transfusions [3] recommends "For operations in critical sites such as the brain or eyes, the platelet count should be raised to 100 x 10^9/L"

THERAPEUTIC PLATELET TRANSFUSIONS

	Platelet Transfusion Threshold				
	20	50	75	100	Individualised threshold
Bleeding, not otherwise specified		•			
Acute promyelocytic leukaemia		•			
Acute DIC		•			
Chronic stable thrombocytopenia					•
Multiple trauma				•	
CNS injury				•	
Massive blood loss/ transfusion			•		

Acute Promyelocytic Leukaemia (APL)

BCSH Guidelines for management of acute myeloid leukaemia [7] recommend that *"The platelet count should be maintained at > 50 x 10^9/L, together with fresh frozen plasma (FFP) and cryoprecipitate to normalise the activated partial thromboplastin time and fibrinogen levels" in patients who are bleeding.*

DIC (Disseminated Intravascular Coagulation)

BCSH Guidelines for platelet transfusions [3] recommend a platelet count > 50 x 10^9/L in acute DIC associated with bleeding.

Chronic stable thrombocytopenia

BCSH Guidelines for platelet transfusions [3] recommend *"A specific threshold for transfusion may not be appropriate for patients with chronic stable thrombocytopenia who are best managed on an individual basis depending on the degree of haemorrhage"*

Multiple trauma

BCSH Guidelines on the management of massive blood loss [17] recommend *"A higher target level of 100 x 10^9 platelets/L..for those with multiple high velocity trauma"*

CNS injury

BCSH Guidelines on the management of massive blood loss [17] recommend *"A higher target level of 100 x 10^9 platelets/L..for those with ...central nervous system injury"*

Massive Blood Loss

BCSH Guidelines on the management of massive blood loss [17] recommend *"A platelet transfusion trigger of 75 x 10^9/L in a patient with ongoing bleeding ...., so as to provide a margin of safety to ensure that the level does not fall below that critical for haemostasis."*

ITP/TTP

BCSH Guidelines for platelet transfusions [3] recommend *"In immune thrombocytopenia platelet transfusions should be reserved for patients with life-threatening bleeding .... In thrombotic thrombocytopenic purpura platelet transfusions are contraindicated unless there is life-threatening haemorrhage, as they have been temporarily associated with exacerbation of TTP."* [3]

APPENDIX 4: OTHER REASONS FOR CHANGING THE PROPHYLACTIC PLATELET TRANSFUSION THRESHOLD

Reasons	No prophylaxis	Threshold 20	Threshold 30	Threshold 50	Other
ITU			1		1*
Recent surgery and ventilation		1			
Hypertension		1			
Rapid fall in platelet count		1			
Dysfunctional platelets				1	
Abnormalities of haemostasis		2			
Neonates			1	1 (pre-term)	1[#]
Terminal patients	1				
CNS tumour					1[#]
Chemotherapy			1		
Bortezomib (Velcade)				1	
Fungal cavity				1	
Splenomegaly		1	1		
Clinical judgement					5[#]
Logistical - due to limited access to platelet concentrates					2[~]
Unknown		2			1[#]

* Clinical judgement [#] No threshold reported [~] Threshold 15

APPENDIX 5: LOCAL DEFINITION OF FEVER

Single Definition (N = 82)

Temperature Threshold (°C)	Number of sites	%		Number of sites	%
37	1	1	Single temperature	0	0
			Sustained temperature	1	1
37.5	8	10	Single temperature	4	5
			Sustained temperature	4	5
38	52	64	Single temperature	44	54
			Sustained temperature	8	10
38.5	21	25	Single temperature	20	24
			Sustained temperature	1	1

Dual Definition (N = 14)

	Sustained temperature			
Single Temperature	37.5	38	38.5	39
37.5	-	-	-	-
38	2	-	-	-
38.5	-	10	-	-
39	-	-	2	-

APPENDIX 6: WHO CLASSIFICATION OF BLEEDING

Grade 1
- Petechiae/purpura that is localised to 1 or 2 dependent sites, or sparse/non-confluent
- Oropharyngeal bleeding, epistaxis <30 minutes duration

Grade 2
- Melaena, haematemesis, haemoptysis, fresh blood in stool, musculoskeletal bleeding or soft tissue bleeding ***not requiring red cell transfusion within 24 hours of onset and without haemodynamic instability***
- Profuse epistaxis or oropharyngeal bleeding *i.e. >30 minutes in continuous duration*
- Symptomatic oral blood blisters *i.e. bleeding or causing major discomfort*
- Multiple bruises, each >2cm or any one >10cm
- Petechiae/purpura that is diffuse or numerous, or >5 distinct purpuric lesions
- Visible blood in urine
- Abnormal bleeding from invasive or procedure sites
- Unexpected vaginal bleeding saturating more than 2 pads with blood in a 24hr period
- Bleeding in cavity fluids evident macroscopically
- Retinal haemorrhage without visual impairment

Grade 3
- Melaena, haematemesis, haemoptysis, haematuria - including intermittent gross bleeding without clots, abnormal vaginal bleeding, fresh blood in stool, epistaxis and oropharyngeal bleeding, bleeding from invasive sites, musculoskeletal bleeding, or soft tissue bleeding ***requiring red cell transfusion specifically for support of bleeding within 24 hours of onset and without haemodynamic instability***
- Bleeding in body cavity fluids grossly visible
- Cerebral bleeding noted on CT (computerised tomography) without neurological signs and symptoms

Grade 4
- Debilitating bleeding including retinal bleeding with visual impairment*
- Non-fatal cerebral bleeding with neurological signs and symptoms
- Bleeding associated with haemodynamic instability (hypotension, >30mmHg change in systolic or diastolic BP)
- Fatal bleeding from any source

**visual impairment is defined as a field deficit, and patients with suspected visual impairment require an ophthalmic consultation*