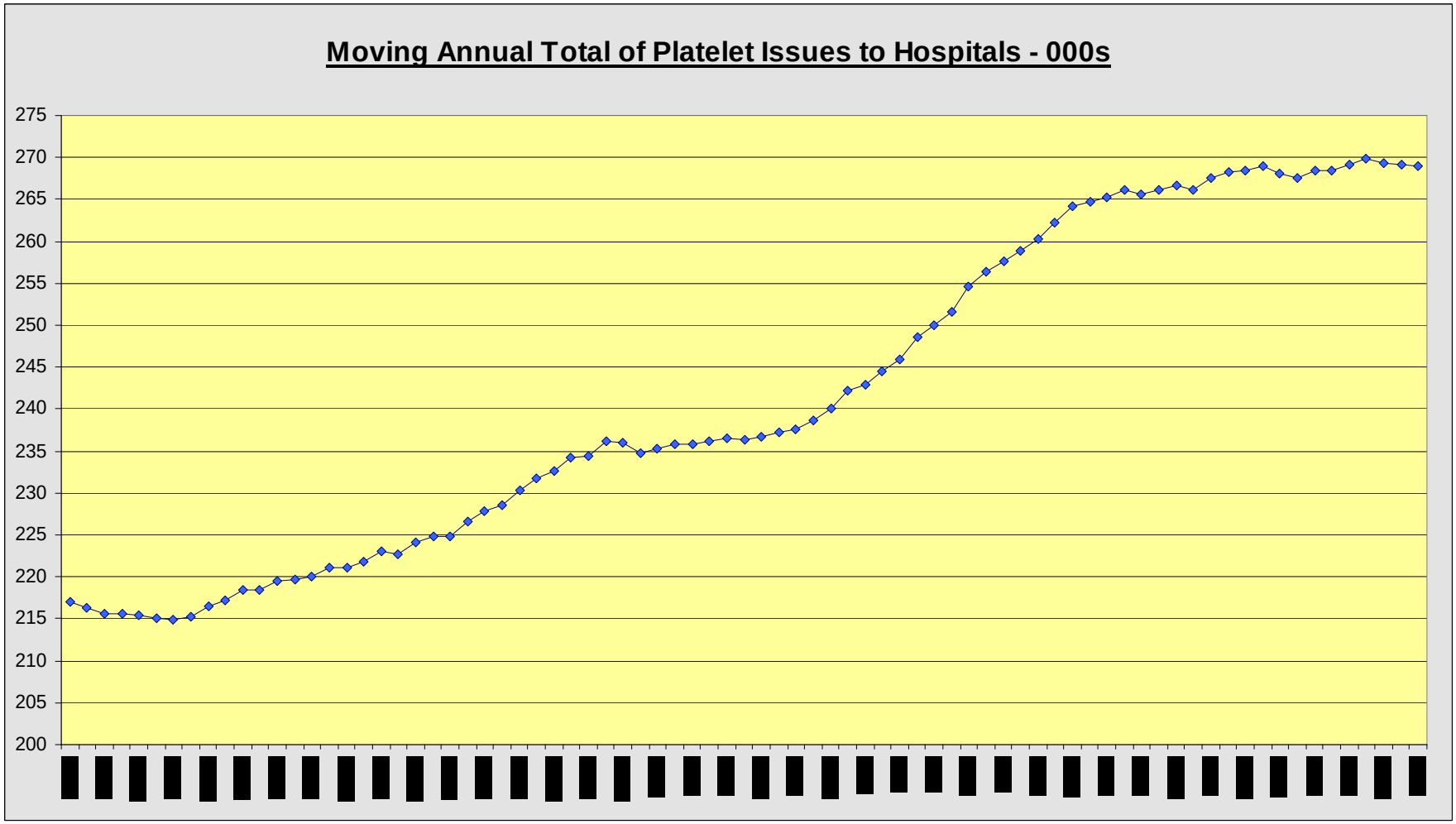
Transfusion indications Part 2: platelets and frozen components

Paula Bolton-Maggs

Platelets

CHANGE IN PLATELET USAGE 2007-2013



Low platelet count

- What is the first question?
- Make a diagnosis!
- Why?
- Because in some circumstances a platelet transfusion is
  - The wrong treatment and
  - It may be dangerous

Clinical implications – make a diagnosis!

- Number
  - Treatment of thrombocytopenia depends upon the cause
  - Name 3 conditions where you would not transfuse platelets
- Function
  - Uraemia
  - Drugs
  - Congenital disorders

Low platelet count

- What patients are at risk of bleeding?
- Fewer than you might think!
- It depends on the cause and associated medical problems

Platelet transfusions

- To prevent spontaneous bleeding in bone marrow failure
- Massive blood transfusion
- Acquired platelet dysfunction
- Inherited platelet disorders
- Immune thrombocytopenia

(handout)

Platelets

- To prevent spontaneous bleeding in patients on treatment that affects their bone marrow
- To help stop bleeding in trauma / obstetric haemorrhage / theatre
- Threshold
  - For prophylaxis 5–10x10^9/l
  - Prophylaxis if septic >20
  - Pre-op minor surgery >50
  - In major surgery / trauma >75
  - In neurosurgery / head trauma >100

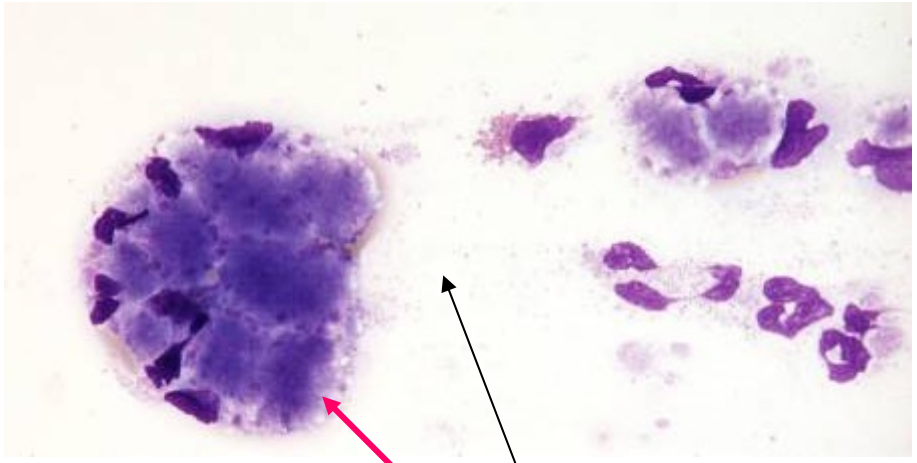
Platelet transfusion: indications

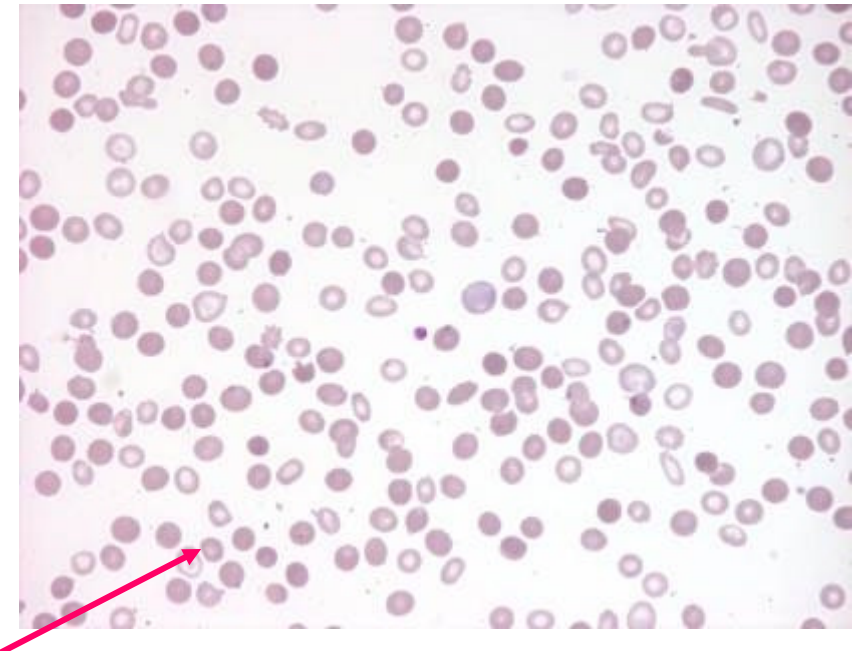
- Bone marrow failure, prophylaxis :
  - P1: p <10 x 10^9/l, stable patient (not indicated in chronic stable patient)
  - P2: p <20 x 10^9/l, additional risk factors
  - P3: p <50 x 10^9/l, invasive procedures (pl <100 x10^9/l, critical sites)
- Critical care/surgery
  - P4: p maintain >75 x 10^9/l, massive transfusion (1.5-2 BV)
  - P5: acquired platelet dysfunction
  - P6: acute DIC with bleeding + severe thrombocytopenia
  - P7: inherited platelet dysfunction with bleeding or as prophylaxis
- Immune thrombocytopenia
  - P8: autoimmune, if major haemorrhage
  - P9: post-transfusion purpura, only if major haemorrhage
  - P10: neonatal alloimmune thrombocytopenia - for bleeding or prophylaxis to maintain p> 30 x 10^9/l

Case 1: Red cells administered instead of platelets

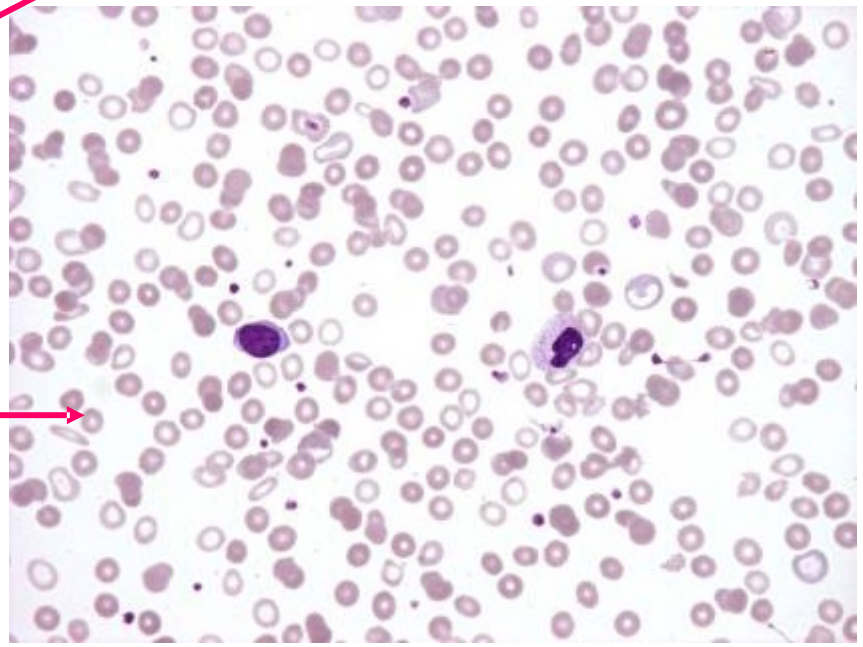
- A unit of platelets was prescribed for administration overnight, with a further unit of red cells to be given in the morning.
- Although the staff nurse believed she had given a unit of platelets, she had collected and transfused a unit of red cells, administering the component over 50 minutes as per the platelet prescription.
- ***What is the risk here?***
- The prescription form was completed with confirmation of bedside checks.
- When questioned, the nurse stated she did not know the difference between a bag of red cells and a bag of platelets.

Post op aortic valve replacement
Platelet count 4 x 10^9/l





Platelet clumps at tail of film
No platelets in smears
(EDTA)



Fresh film made at bedside
Normal numbers of platelets

Case 2

Helpful nurses and doctor administer platelets to the wrong patient

- Platelets arrived in ITU and sister took them a patient's bedside. This was not the bedside of the patient to be administered platelets.
- However, finding the patient unconscious and without an ID bracelet she went to write a wristband.
- Two other nurses saw the platelets and checked them by asking other staff if it was the correct patient.
- Finding the platelets were not written up for that patient, they asked the doctor to prescribe them, which he did.
- The platelets were then given to this patient who did not require them, but they were for another patient on the unit. There was no adverse reaction.
- ***What were the errors here?***

Case 3: Failure to prepare for predictable thrombocytopenia contributes to death

- A 62 year old man died from haemorrhage and sepsis. He was receiving chemotherapy for malignant disease resulting in a falling platelet count. A group and screen sample was not sent in a timely manner despite the predictable fall in count so that platelets were not available and prophylaxis was not given when indicated at the threshold platelet count ($<10x10^9/L$)
- Inadequate junior medical staffing levels and supervision were cited as contributory factors (2 errors)

National comparative audit of blood transfusion

- A programme of clinical audits looking at use and administration of blood and blood components in England and N Wales
- Funded by the NHSBT
- Started 2003, in collaboration with the clinical standards unit of the RCP

www.nhsbtaudits.co.uk

National Comparative Audit of the use of Platelets 2007

Invited

- 279 NHS hospitals
- 74 Independent hospitals

Who took part

- 182 (65%) NHS hospitals returned information
- 5 (7%) Independent hospitals returned information

Number of transfusions audited

- Nationally = 4421 North West RTC = 700

National Comparative Audit of the use of Platelets

The Audit Results

- 4,421 transfusions audited (>89% of the patients in each clinical category were from hospitals in England)
- Reason for transfusion found for 93%
- 57% were prophylactic transfusions in the absence of bleeding (in line with previous data)
- No platelet count before transfusion in 29%

Use of platelets in haematology

2,125 cases from 174 hospitals, median 13 per site

- 55% received platelets for prophylaxis
- 26% had bleeding
- 12% were given prior to invasive procedure
- 7% - no reason for platelet transfusion was stated

Use of platelets in haematology

Standard:

–Threshold for prophylactic transfusion is a platelet count $\leq 10 \times 10^9$/L,

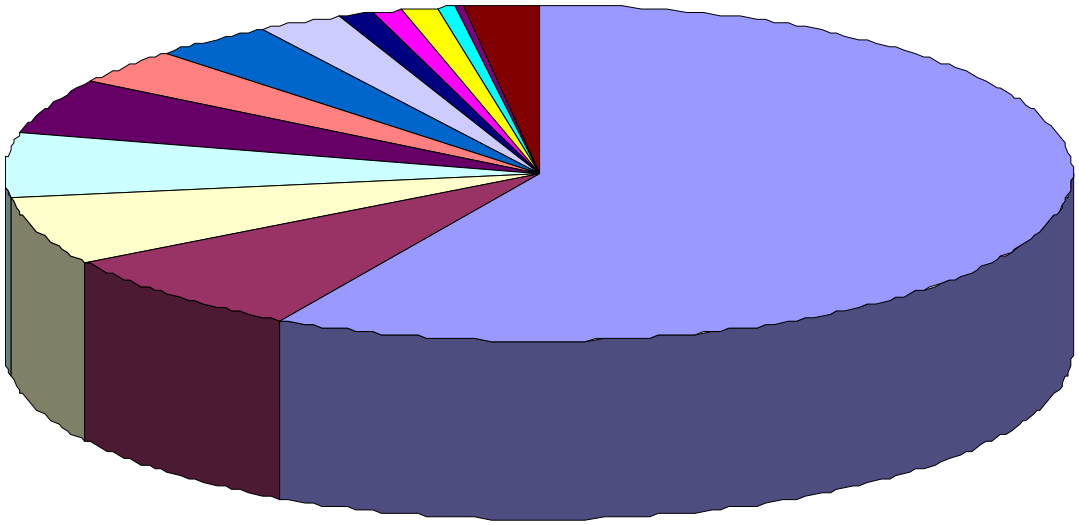
–or $<20 \times 10^9$/L if sepsis (on i.v. antibiotics or antifungal therapy), APML or abnormal coagulation (BCSH, 2003)

Conclusions

- Significant lack of compliance with BCSH guidelines
- Majority of non-compliant transfusions in haematology patients were in the prophylactic category
- Appropriate use should reduce healthcare costs, improve platelet availability, and reduce risks to patients

Where do platelets go ?

NW RTC 2010 - 1550 platelet issues



- Haematology 58%
- ICU 8%
- Cardiac Surgery 6.5%
- Oncology 6.3%
- General Medicine 5.4%
- General Surgery 3.7%
- SCBU 3.5%
- GastroIntestinal 2.5%
- Emergency Dept 1%
- Obstetrics 1%
- Neurosurgery 1%
- Orthopaedics 0.5%
- Urology 0.5%
- Others 2%

Repeat national comparative audit of platelet transfusions in haematology patients 2010

60% aged 60 yrs or older, 7% <18 yrs
AML 29%, lymphoma 18%, MDS 11%
1% (42/3296) had reaction to transfusion

Results

- Inappropriate transfusions in 28% (915/3296) measured against BCSH guidelines
- 69% (2283/3296) for prophylaxis
  - 34% (782/2283) inappropriate
  - 26% (602/2283) transfused above recommended thresholds
- 10% (220/2277) of prophylactic transfusions were double dose

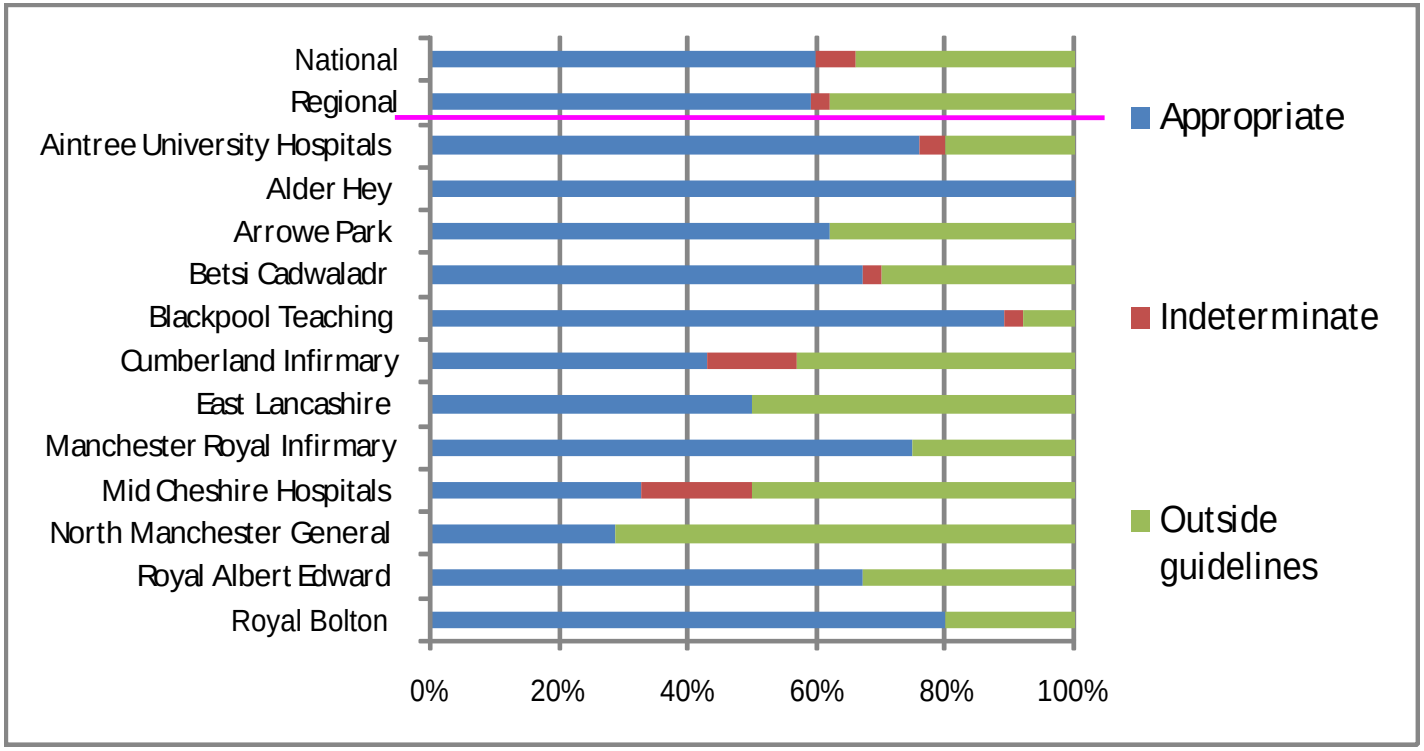
Results - 2

- Pre-invasive procedure – 15% (497/3296)
  - 23% (114/497) inappropriate
  - 9% (45/497) before bone marrow trephine
  - 14% (69/497) too high a threshold
- Therapeutic transfusions – 13% (412/3296) and <5% (19/412) inappropriate (these were patients with ITP or TTP with non-life-threatening bleeds

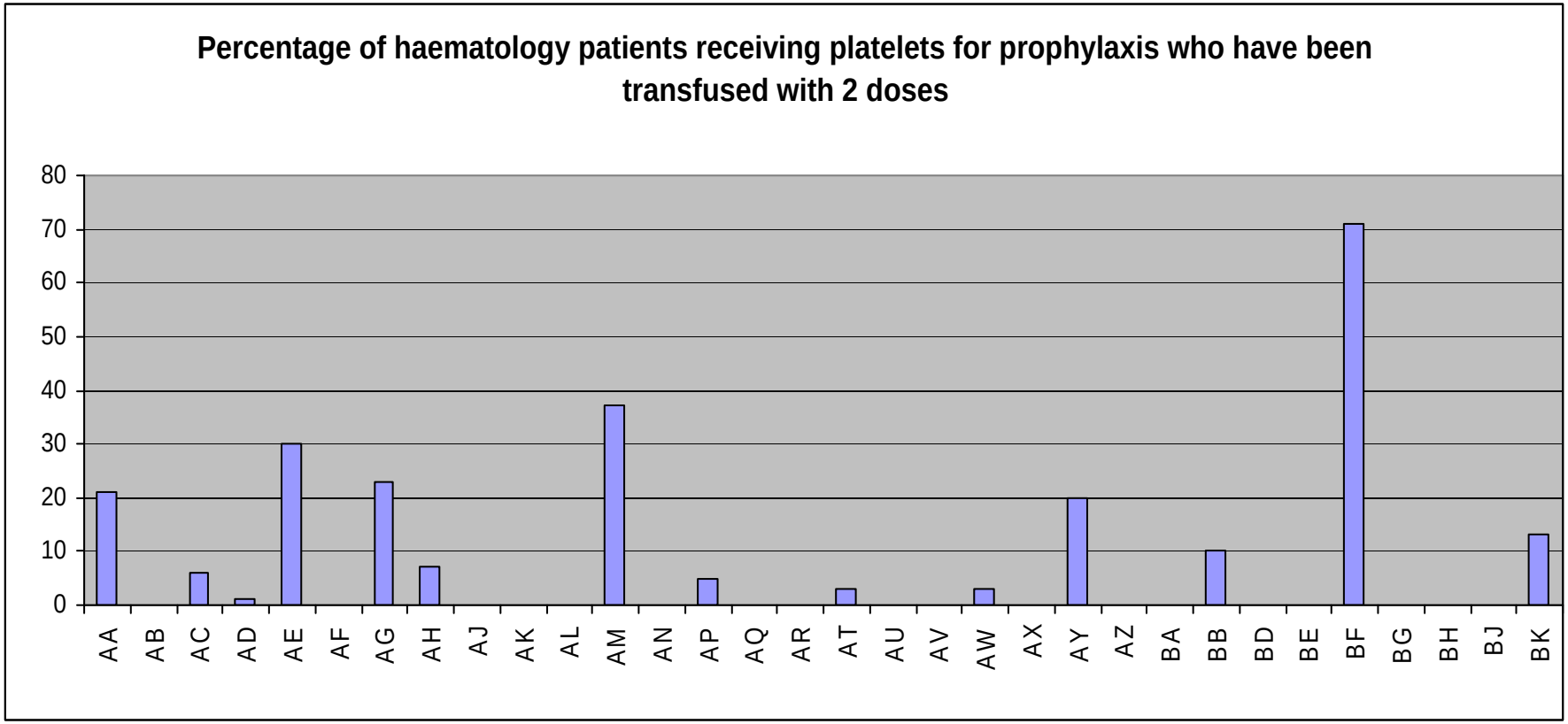
Evidence of inappropriate use

Appropriateness of prophylactic transfusions

NHS Blood and Transplant



Evidence of inappropriate use



NW RTC Platelet Audit 2010

Case 4

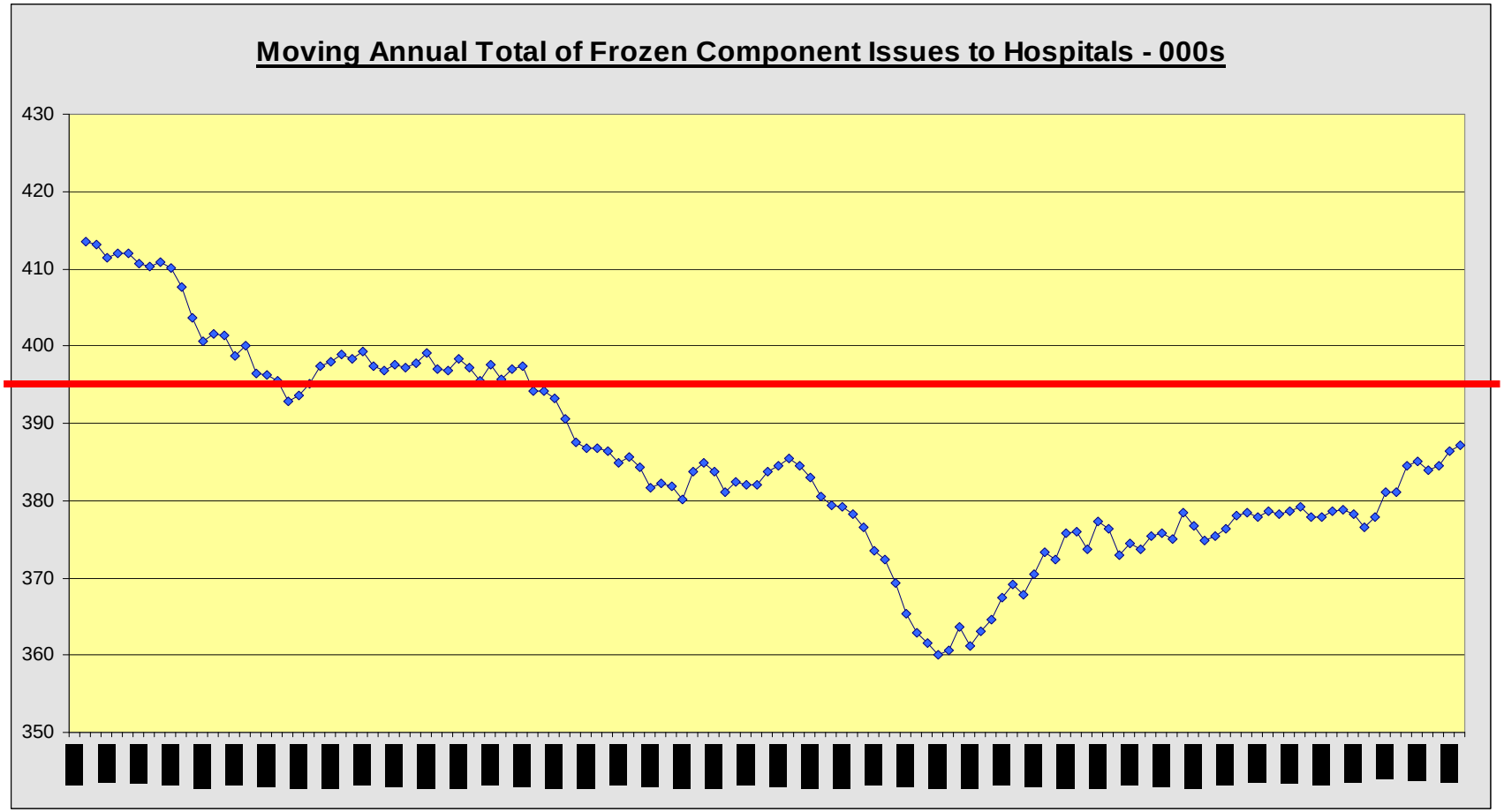
- A middle-aged male developed oozing following coronary artery bypass grafting and was transfused with a platelet pool. He was already on invasive ventilation on ITU at this time.
- ***Is this an appropriate transfusion?***
- He became hypoxic (pO2 9.7 kPA), hypercapnic and hypotensive within 50 minutes of transfusion. He was afebrile with a normal central venous pressure (CVP) level and his electrocardiogram (ECG) showed sinus tachycardia only.
- His echocardiogram (ECHO) showed poor right ventricular function and CXR showed bilateral infiltrates. He remained on mechanical ventilation for 3 days, following which he made a full recovery.
- ***What is the diagnosis?***
- TRALI follows receipt of platelet pool suspended in female donor plasma

Frozen components

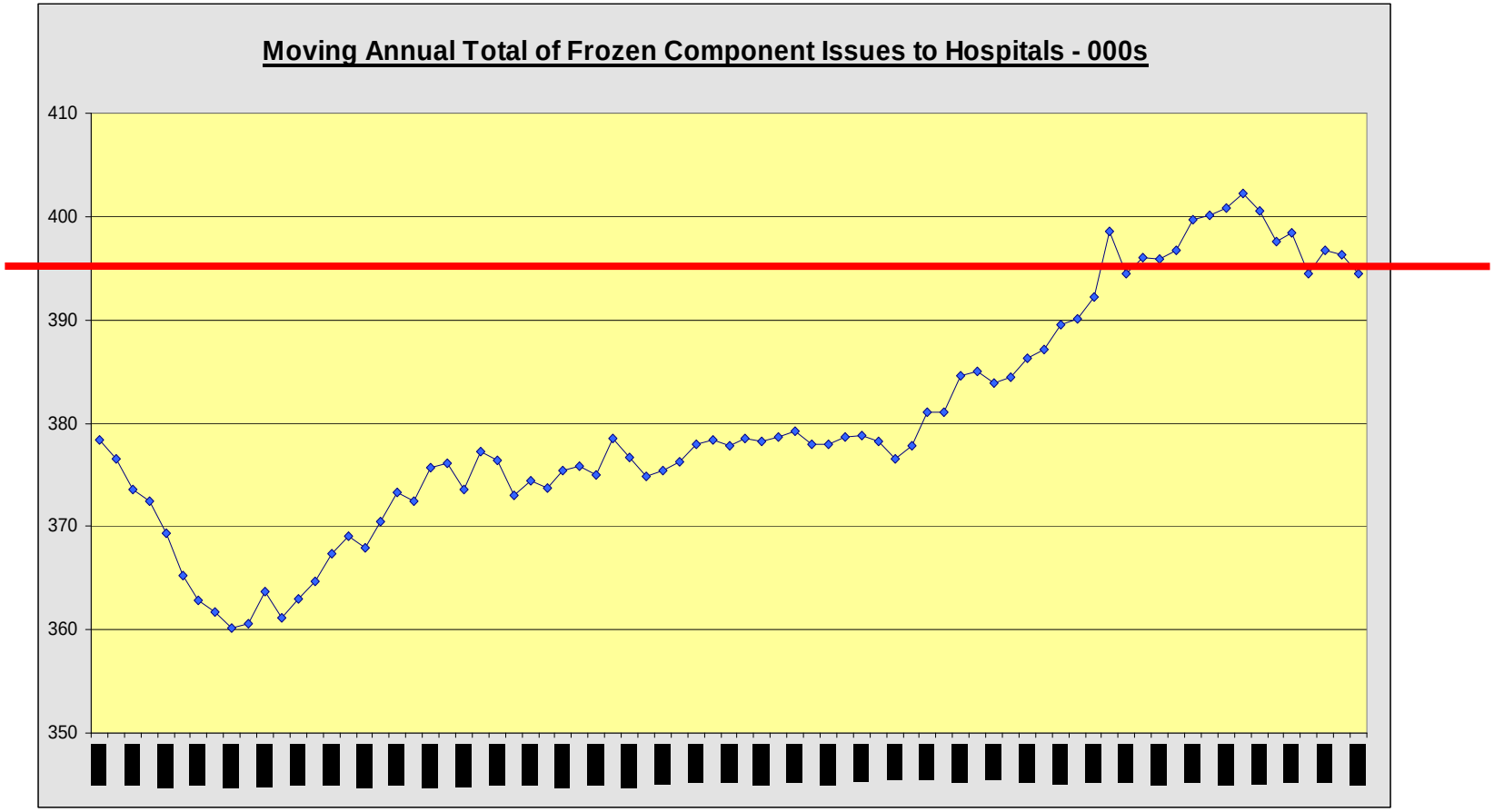
Fresh Frozen Plasma

- Increasing concern because of vCJD risk
- Importation of plasma for fractionation (1998) and selected clinical use (2003)
- Still evidence of increasing use
- Dose at 15-20 ml/kg
- Audit consistently shows
  - 33% we get it about right
  - 33% we give it inappropriately
  - 33% we don’t give enough

FROZEN COMPONENT ISSUES 2001-2011



FROZEN COMPONENT ISSUES 2007-2013



FFP

- When might you order this?
- What group of FFP is safe for everybody?

Indications for FFP are few

15mL/kg

F1 Replacement of single coagulation factor deficiencies where a specific or combined factor concentrate is unavailable (e.g. factor V deficiency)

F2 Immediate reversal of warfarin, in the presence of bleeding only when PCCs not available. FFP has a partial effect and is not the optimum treatment

F3 Acute DIC in the presence of bleeding and abnormal coagulation results

F4 Thrombotic Thrombocytopenic Purpura, usually in conjunction with plasma exchange

F5 Major haemorrhage (ratio 0.5 FFP to 1 unit RBC)

F6 Liver disease; there is no evidence of benefit for FFP in non-bleeding patients regardless of the PT ratio

Cryoprecipitate

- Contains higher levels of Fibrinogen and FVIII than FFP
- Trigger level is <1.5g/L if bleeding, or higher in obstetric patients
- Standard dose is 2 pools (5 donations in each)
  - ~3.5g fibrinogen
- Fibrinogen concentrate available but restricted license

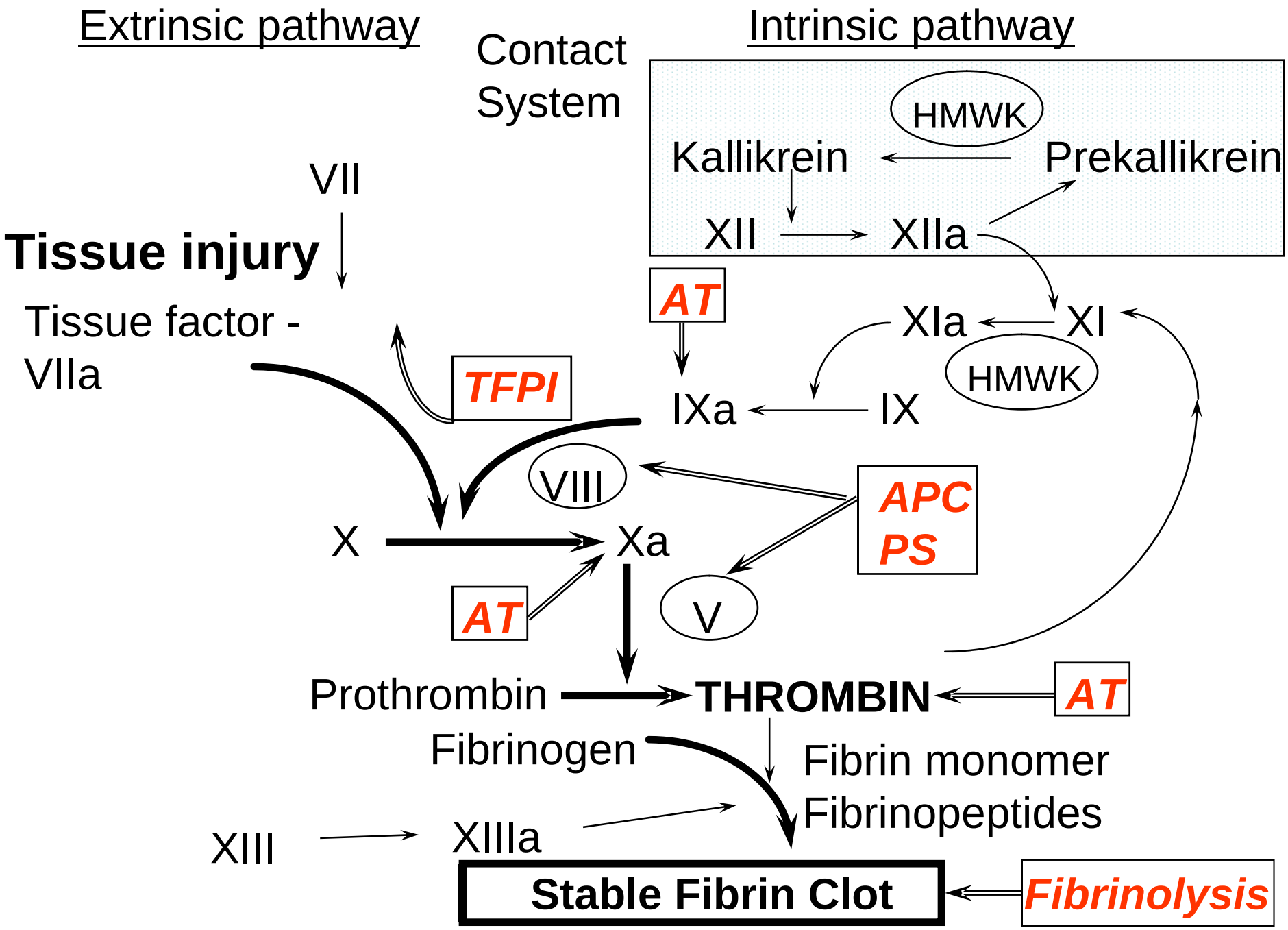
Cryoprecipitate

- To replace fibrinogen
- Seek advice from a haematologist
- Allow 30 minutes to thaw
- Dose 1-2 pools in an adult * then review
- Must be transfused through a 200 micron filter (blood administration set)

**Units now supplied in pools of 5 as well as singly*

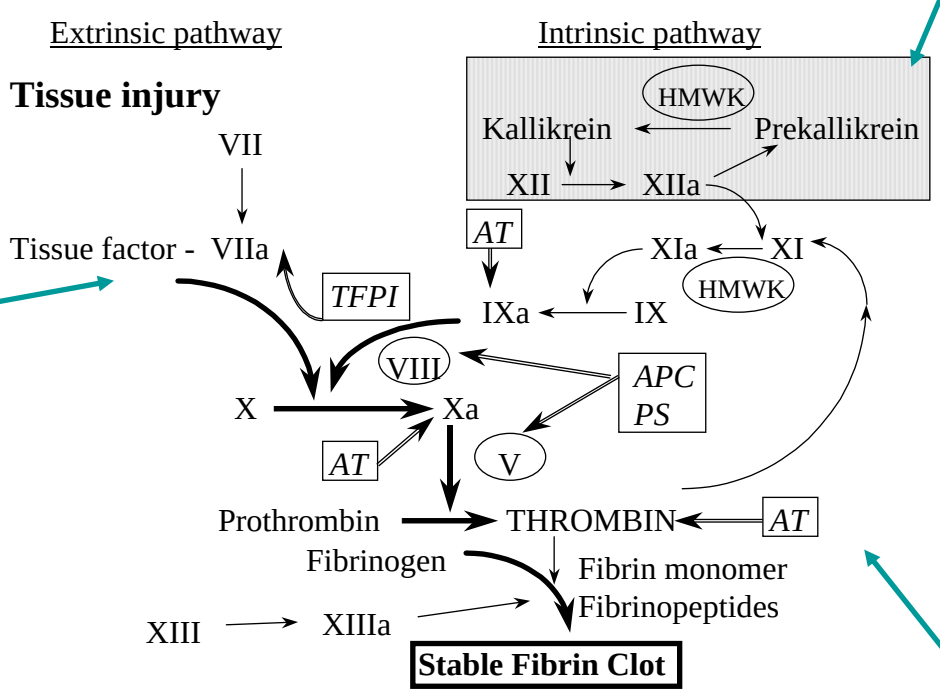
Coagulation tests

may tell us very little
can be misleading


Extrinsic pathway
Contact System
Intrinsic pathway
HMWK
Kallikrein
Prekallikrein
VII
XII
XIIa
Tissue injury
AT
Tissue factor - VIIa
XIa
XI
TFPI
HMWK
IXa
IX
VIII
APC
PS
X
Xa
AT
V
Prothrombin
THROMBIN
AT
Fibrinogen
Fibrin monomer
Fibrinopeptides
XIII
XIIIa
Stable Fibrin Clot
Fibrinolysis

The contact system –
No role in coagulation – makes the APTT long
Important in inflammation

The degree of tissue factor expression on different cells at different times is crucial

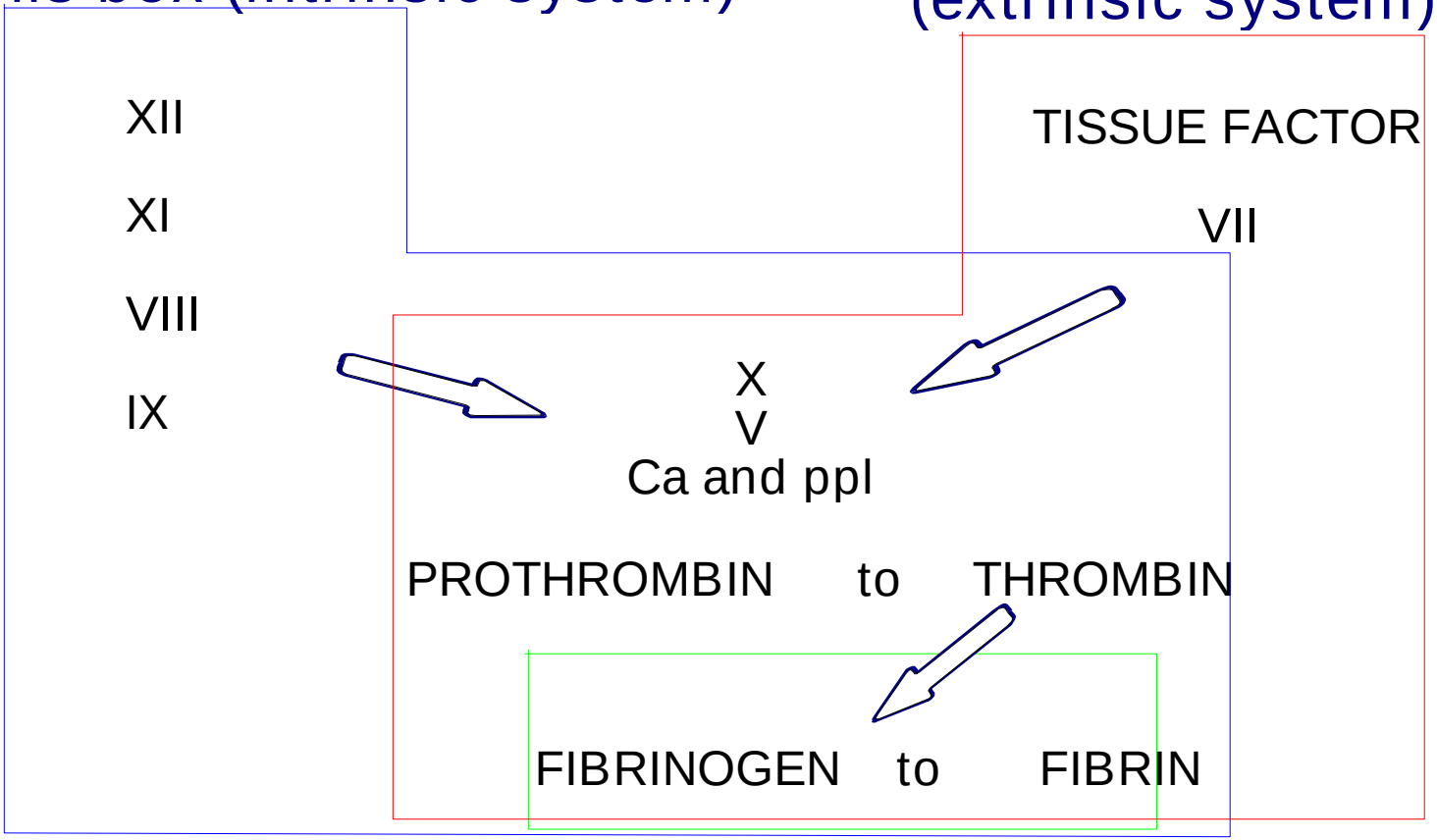


AT needs heparin-like molecules for maximum activation

ESSENTIALS OF COAGULATION - WHAT ARE THE TESTS

APTT - looks at everything in this box (intrinsic system)

PT - looks at everthing in this box (extrinsic system)



Thrombin time - TT - only looks at this conversion.

Inadequacies of tests

- No information about the anticoagulants
- No information about fibrinolysis
- Very dependent on sample and technique of venepuncture
- The APTT is very sensitive
- Lupus anticoagulants are quite common and associated with thrombosis

Assumptions in Pre-Procedure Treatment

- Elevated PT (INR), APTT *predicts* bleeding
- NO

- 2-4 units of FFP will correct the abnormality
- NO

- Treatment before a bleed is more effective than treatment after a bleed
- NO

FFP NOT indicated

- Hypovolaemia
- Plasma exchange **except for** Thrombotic Thrombocytopenic Purpura (TTP)
- Formula replacement (‘had 4 units blood’) except possibly for major haemorrhage

Reversal of Warfarin

- Vitamin K preferable in absence of serious bleeding – if given IV correction maximal in 4 - 6 hours, half-life 18 hours. Oral takes longer, more than 12 h
- If bleeding, Prothrombin Complex Concentrate (PCC) (Octaplex/Beriplex), together with Vitamin K
- PCC contains factors II, VII, IX and X

Evidence of inappropriate use

The use of fresh-frozen plasma in England: high levels of inappropriate use in adults and children

Simon J. Stanworth, John Grant-Casey, Derek Lowe, Mike Laffan, Helen New, Mike F. Murphy, and Shubha Allard

In adults 43% of FFP transfusions were given in absence of documented bleeding as prophylaxis for abnormal coagulation tests or before procedures or surgery
– in 30% 0f these the INR was 1.5 or less
14% of all FFP transfusions were for reversal of warfarin
In 40% of transfusion episodes the dose was < 10ml/ kg

TRANSFUSION 2011;51:62-70.

National Comparative Audit of the use of Fresh Frozen Plasma 2009

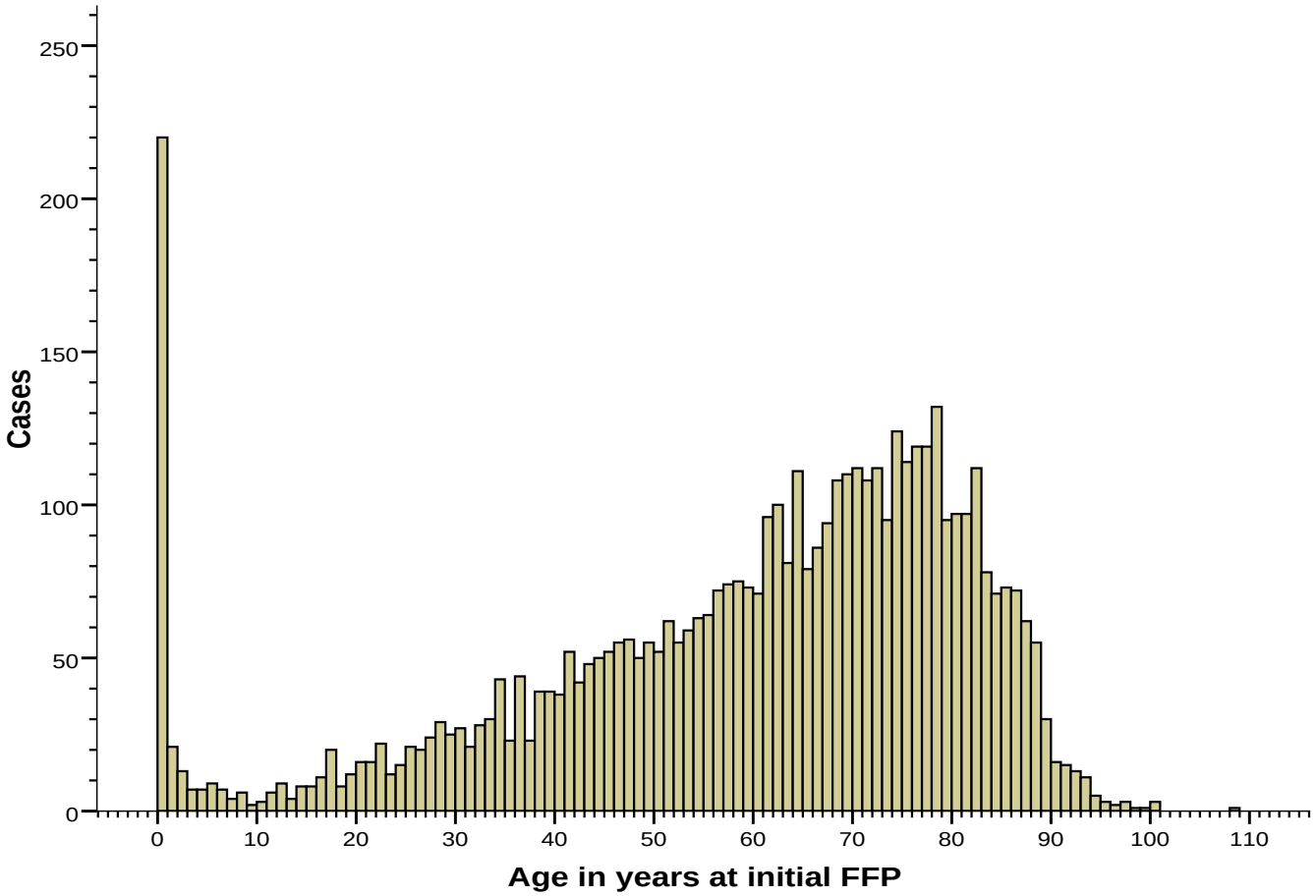
North West RTC

Prepared by
John Grant-Casey
on behalf of the NCA FFP
Project Group

April 2009

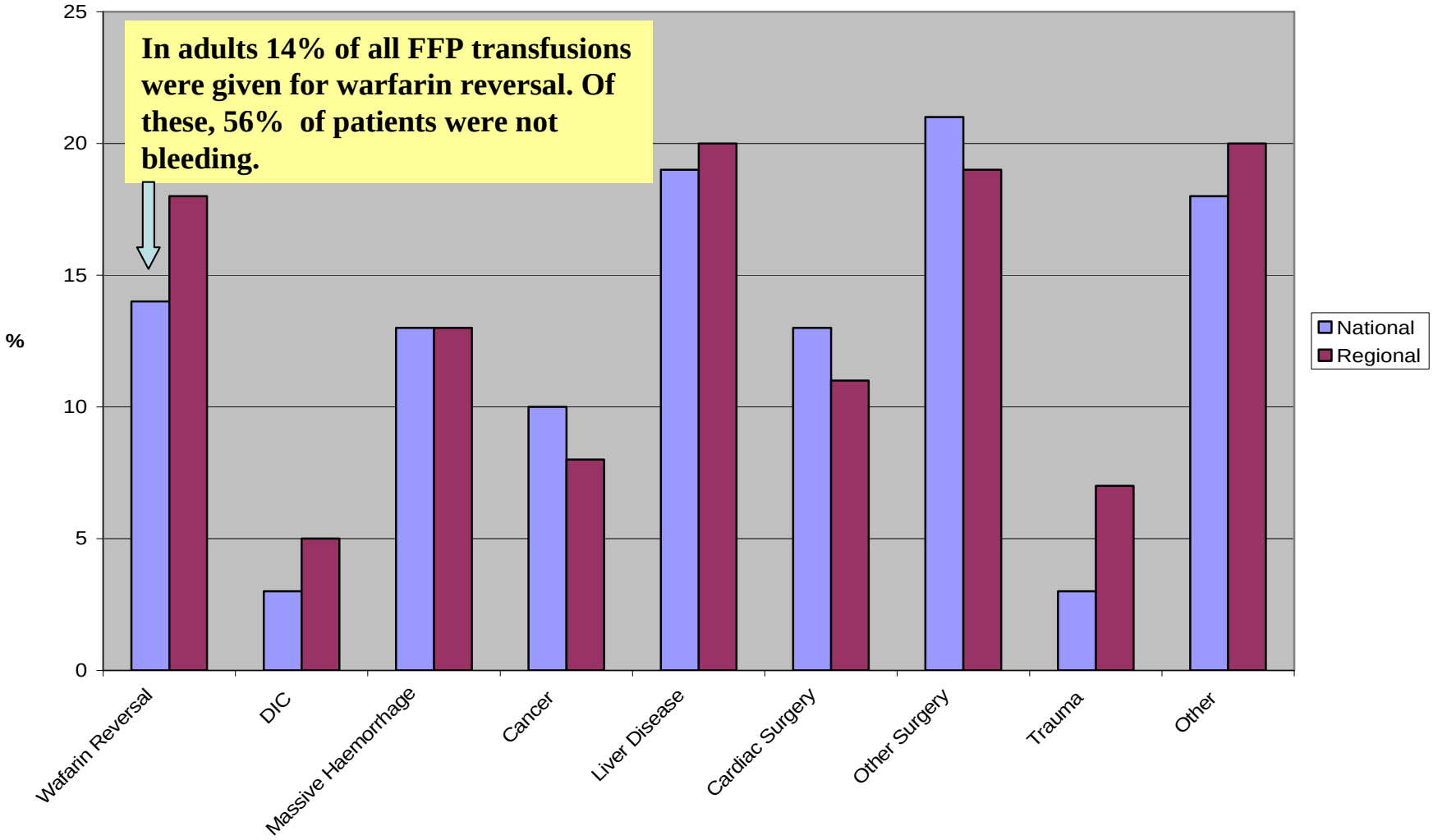
Use of FFP

Age ranges: 4635 - 16+;
114 - 1-15 years;
220 < 1 year old



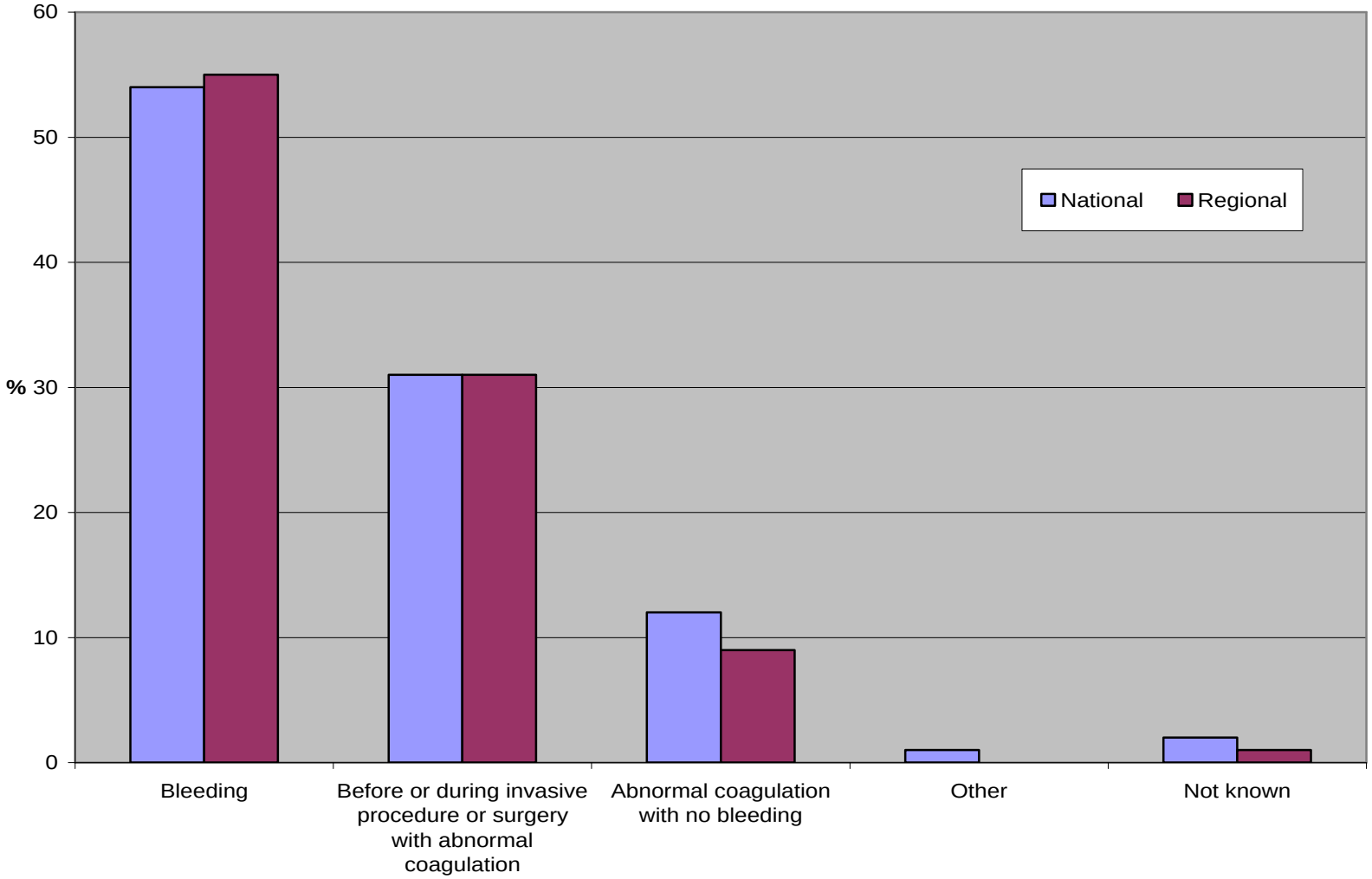
Use of FFP

Underlying medical or surgical conditions in Adults



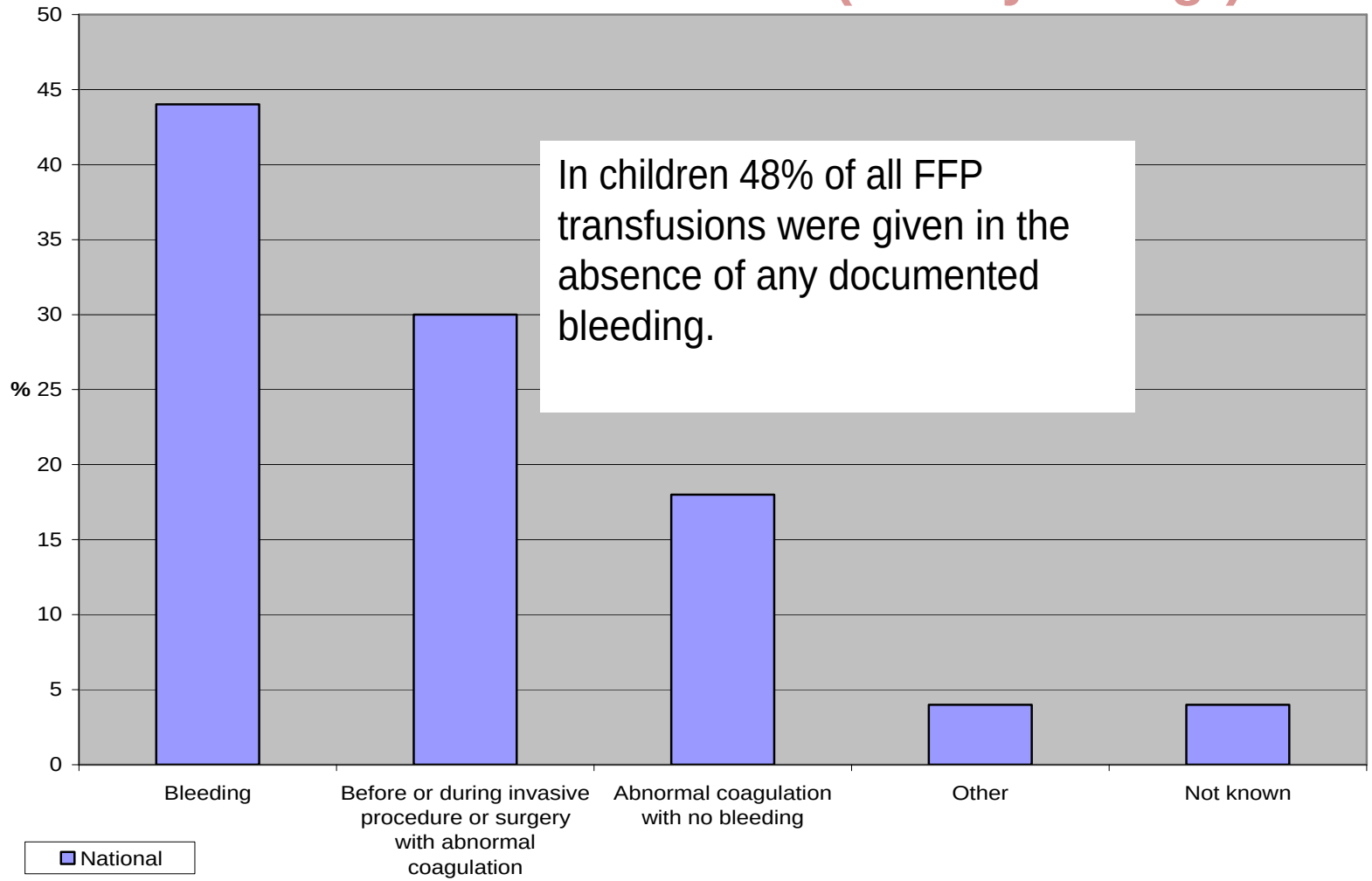
Use of FFP

Main reason for transfusion in Adults



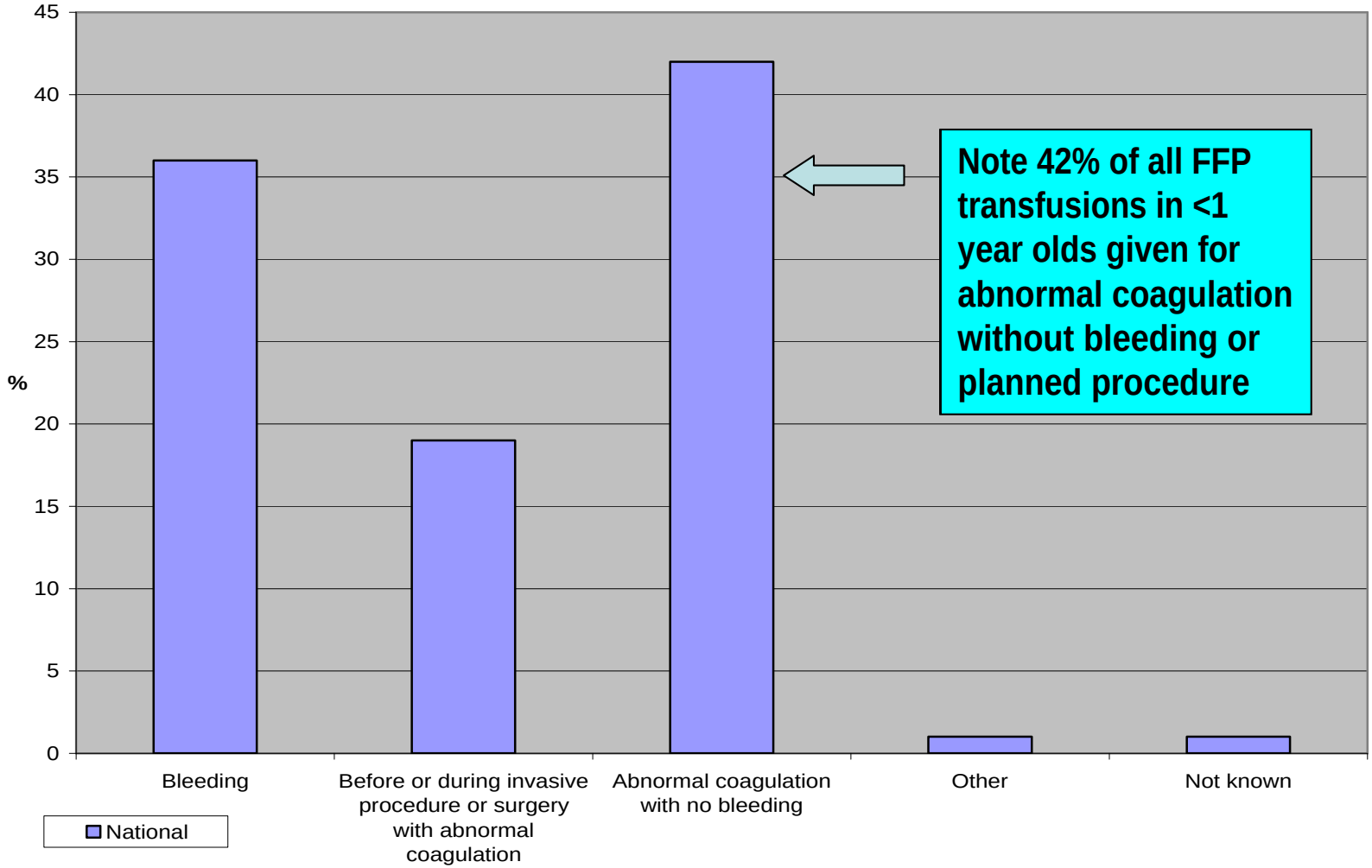
Use of FFP

Main reason for transfusion in Children (1 – 15 yrs of age)



Use of FFP

Main reason for transfusion in Infants (< 1 year old)



Other key results

Dose of FFP used

- There was wide variation in FFP dose transfused by weight.
- The median overall dose was:
  - Adults 11ml/kg.
  - Children 12ml/kg.
  - Infants 14ml/kg.
- In 40% of adults (873/2186) the dose was less than 10ml/kg.
- The therapeutic dose is considered to be 15-20ml/kg

Documentation in case notes

- The reason for transfusion was not documented in the case notes for 28% of adults, 24% of children and 17% of infants.

Cryoprecipitate

- What is it?
- When might we use it?

Other key results

Use of Cryoprecipitate

- Cryo also given to 10% of adults, 13% of children and 15% of infants within 24 hours of receiving the first FFP transfusion.
- Of these, 67% of adults, 64% of children and 35% of infants had fibrinogen levels of ≥ 1.0g/l.

Reference ranges for neonatal coag results

- 32% (56/176) of centres used separate laboratory reference range for neonatal patients

Audit Recommendations

- Widespread use of FFP for prophylaxis needs careful scrutiny - audit has shown that many non-bleeding patients with normal or only minor derangements of PT or INR were given FFP.
- Much FFP use results in minimal or no improvement or correction in coagulation abnormalities.
- High quality trials are needed to address the question of efficacy of FFP use particularly in non-bleeding patients.

Recommendations -1

- Trusts/ Hospitals should have local guidelines for FFP use for adult and paediatric patients based on BCSH guidelines and including indications where pathogen inactivated plasma should be used
- The dose of FFP should be in accordance with BCSH guidelines
- The indication for FFP use must be documented in the case notes
- Appropriate reference ranges should be used when reporting coagulation results in neonatal patients

Recommendations - 2

- FFP use should be guided by coagulation test results – empirical use in massive haemorrhage should be confined to recommendations as stated in local guidelines
- Trusts / Hospitals should empower transfusion laboratory staff to challenge medical staff about the issue of FFP where no clear clinical indication as defined by local guidelines
- Prothrombin Concentrate Complex (PCC) should be the treatment of choice for the reversal of warfarin overanticoagulation

Some more case examples

Case 5

- A GP refers in an asymptomatic 30 yr old woman with menorrhagia and Hb 44g/L
- ***What would you do?***

Case 6

- A consultant ‘thought that the patient was RhD negative’ and prescribed 500 IU anti-D Ig following a potentially sensitising event.
- The anti-D Ig was issued from a remote clinical stock and administered.
- ***What should have happened?***
- At no point in the process was the blood group report ever checked – it showed clearly that the patient was RhD positive.
- ***Anti-D Ig should never be administered without checking the patient’s blood group***

Case 7

- A nurse was instructed to take a blood sample for transfusion from the patient in Bed 2.
- ***Comments?***
- She was given no documentation and continued to label the sample with the information contained in the notes for that bed number.
- However, it was not appreciated until later that a different patient was now occupying Bed 2 and that the request should have applied to the patient in Bed 3.
- ***Patients identified by bed numbers only***

Case 8

- A patient was in possession of an antibody card, which he showed to the phlebotomist.
- However, this information was not transmitted to the laboratory, the antibody screen was negative and non-phenotyped red cells were issued.
- The patient again presented his card to the nurse at the time of the bedside pre-administration check, following which antigen negative units were issued.
- ***Patient's persistence in showing his antibody card avoids a transfusion of non-phenotyped units***

Case 9

Lack of POCT device knowledge leads to erroneous result and transfusion

- A consultant anaesthetist anaesthetised a child for a procedure. Halfway through surgery it was estimated the patient had a blood loss of approximately 700 mL and he asked the operating department practitioner (ODP) for a POCT Hb estimation.
- The ODP returned from recovery to state that they did not have the model requested but a different model was available. The ODP assumed that this was an alternative device for Hb estimation. It was in fact a device for checking blood sugar.
- The result of 7.2 was consistent with clinical suspicion and the anaesthetist requested blood on this basis. After 100 mL of blood had been transfused the ODP informed him that they had checked with recovery staff and the machine used was for blood sugar testing. The transfusion was stopped and a sample was sent to the laboratory. The result was 11.6 g/dL.

Case 10

Incorrect hospital number – detected but ignored

- An FY1 doctor entered another patient's hospital number on a blood sample for a patient requiring a 4-unit blood transfusion.

- When the nurses questioned the different number on the patient's wristband with the FY1, she requested them to ignore this because the patient urgently needed the blood. (The patient's Hb was 62 g/L)
- ***Is this the right answer?***

- The nurses proceeded to give all 4 units of blood based on another patient's hospital number.

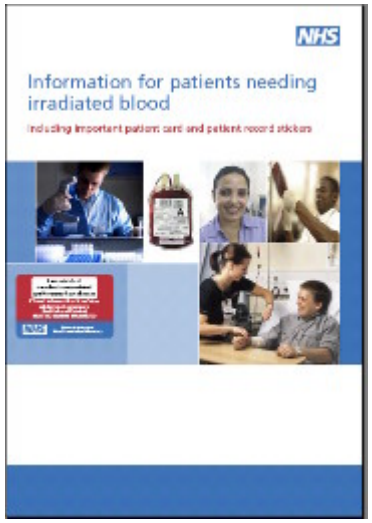
Case 11

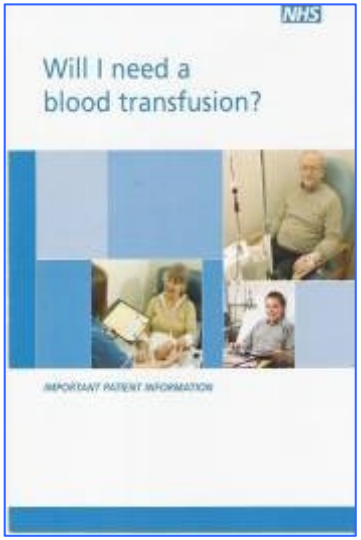
Transfusion based on a year-old haemoglobin result

- Two units of blood were requested for an orthopaedic trauma case because of low pre-op haemoglobin of 97 g/l. The blood was provided and transfused.
- A phone call to the laboratory to check the pre-op Hb result and coagulation screen alerted the staff to the fact that the samples sent had been clotted and therefore could not be analysed.
- The result used to request the transfusion had in fact been taken on exactly the same date, but one year earlier.
- The post-operative Hb was 139 g/L.

Requesting Procedures

- Decision and reason to transfuse recorded in notes
- Communication with the patient
- Explain risks / benefits – patient leaflets





Case 12

- A patient receiving a red cell transfusion complained of severe back pain, and then developed rigors.
- *What would you do next?*
- The deputy Sister attended the patient, noticed it was the wrong blood, took it down and bleeped the junior doctor.
- *What should happen next?*

Case (cont.)

- The ward then phoned Blood Bank requesting a further unit of blood for another patient as the first had been 'wasted'.
- *What does this demonstrate?*
- Only when the BB manager asked for the bag was it revealed that the unit had erroneously been given to the wrong patient.
- BB Mgr contacted a consultant haematologist who went to see patient immediately.
- The sticky label from the blood bag tag had been removed from the medical notes, and the name had been crossed out on the blood bag label. The bag of blood had been thrown into the sharps bin, this was retrieved by consultant haematologist.
- The nurse who put up the blood admitted she had not performed any bedside checks.
- **Worrying lack of comprehension of reasons for standard procedures, and disregard for consequences**

Case 13

Blood transfusion process

- A unit of red cells was commenced on an elderly male patient at 05.30 for acute blood loss.
- *What should happen now?*

- At 20.30 the ward staff contacted the laboratory to say the blood transfusion was still running after 15 hours.

- On investigation it was noted that NO observations had been recorded following the 15 minute post-transfusion check.