

# **BBTS JAMES BLUNDELL AWARD 2017**

Getting the message across: turning  
data into stories

Lorna M Williamson

# **Evidence-based medicine:**

## **‘Let my dataset change your mindset’**

**Hans Rosling, Statistician & Communicator**



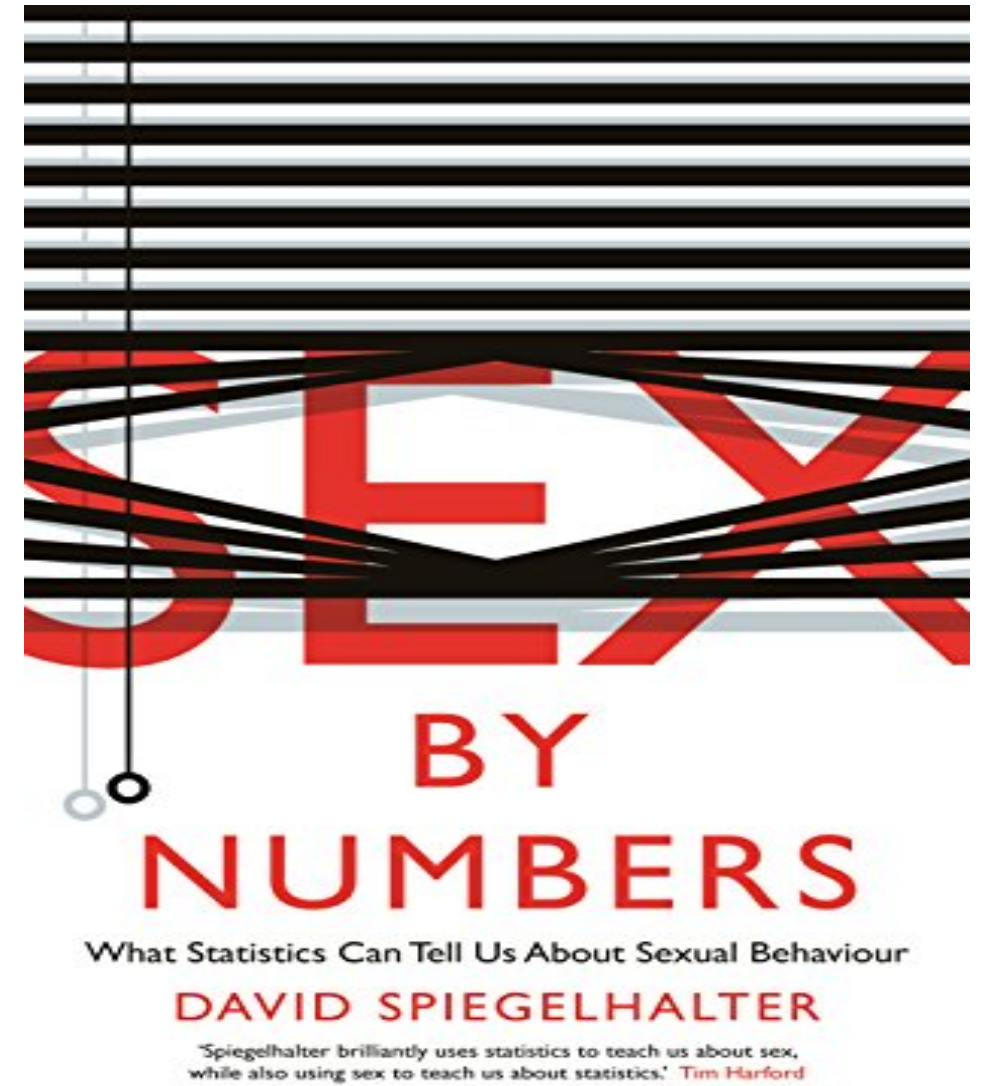
- D. Non-analytic studies: case report, case series, expert opinion
- C. Case control/cohort studies with low risk of bias: SHOT
- B. Systematic reviews of case control/cohort studies
- A. Randomised clinical trial OR systematic reviews of RCTs: CTU

# 1. Grab the audience's attention: numbers or stories?





**Professor Sir David Spiegelhalter**  
**Winton Professor for the**  
**Public Understanding of Risk**  
**University of Cambridge**



1994: 'Would you like to set up UK haemovigilance----?'



Dr Angela Robinson

Medical Director  
NBS England

**SHOT**

- **S**erious
- **H**azards
- **O**f [NOT 'IN']
- **T**ransfusion



Dr Brian McClelland  
SNBTS

***“Right blood, right patient,  
right time”***

Prescription/blood  
sample from patient



Hospital blood bank



Collection from hospital storage site



Administration of blood to the patient



SHOT was affiliated to  
Royal College of  
Pathologists

Professor Sir John Lilleyman  
Chair, Inaugural SHOT Steering Group meeting  
Royal College of Pathologists, December 1995

SHOT launch: 1 October 1996

## **A SHOT in the arm for safer blood transfusion**

*A new surveillance system for transfusion hazards*

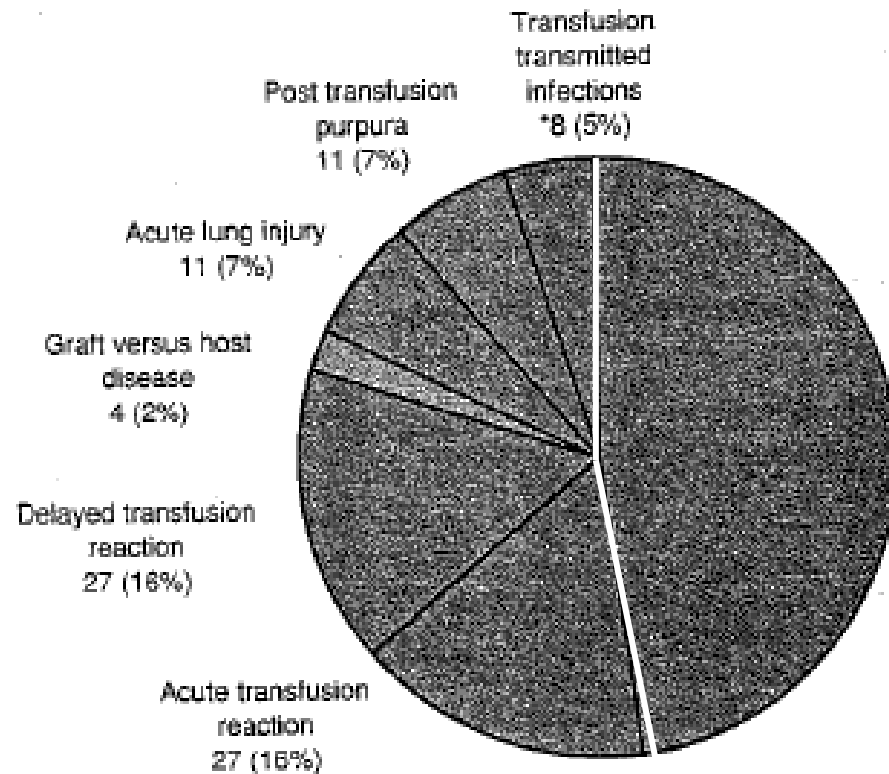
Williamson LM, Heptonstall J, Soldan K. BMJ. 1996 Nov 16;313(7067):1221-2.

**Thanks to Liz Love, Hannah Cohen, Hilary Jones.**

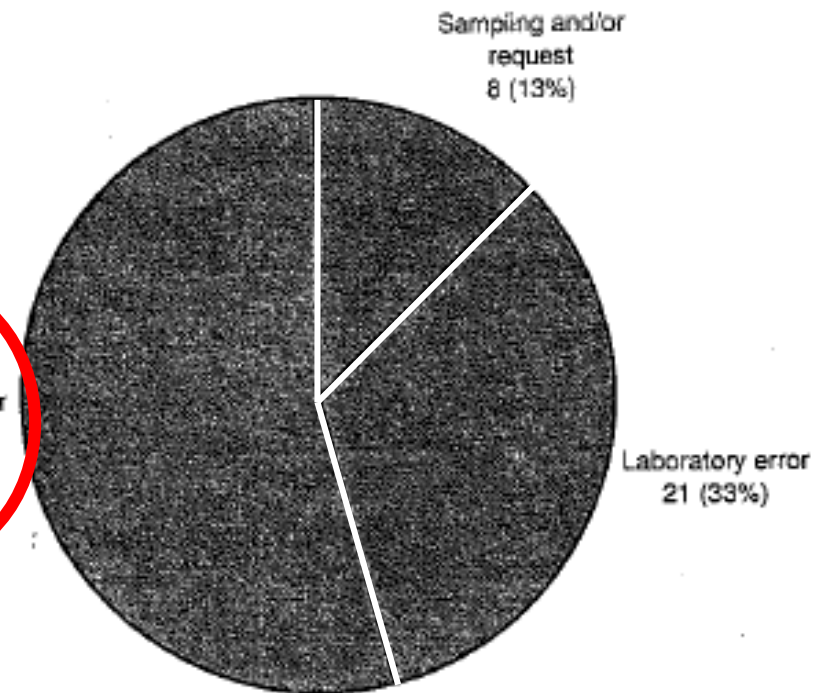
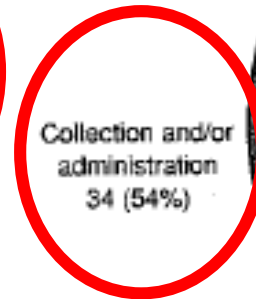
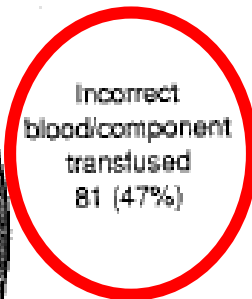


# The first SHOT report 1996-97

169 initial reports (141 completed) from 94 of 424 hospitals



169 cases where initial reports received



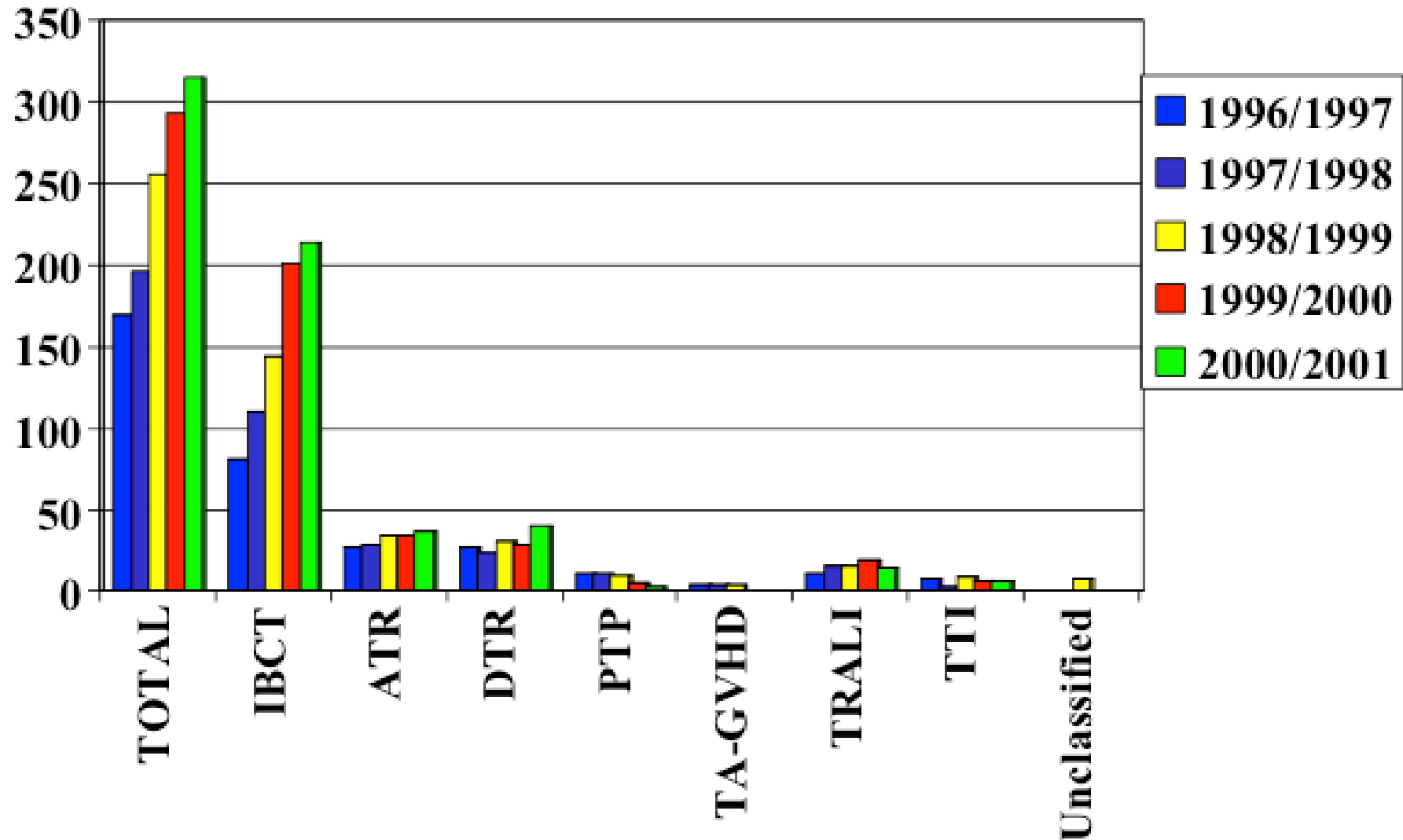
Distribution of errors in completed reports  
(n=63)

**2. Adjust  
your  
content to  
the  
audience.**

**RCPath at  
House of  
Commons**

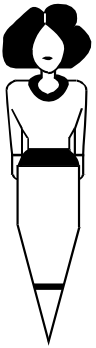


## Comparison of initial reports 1996 - 2001

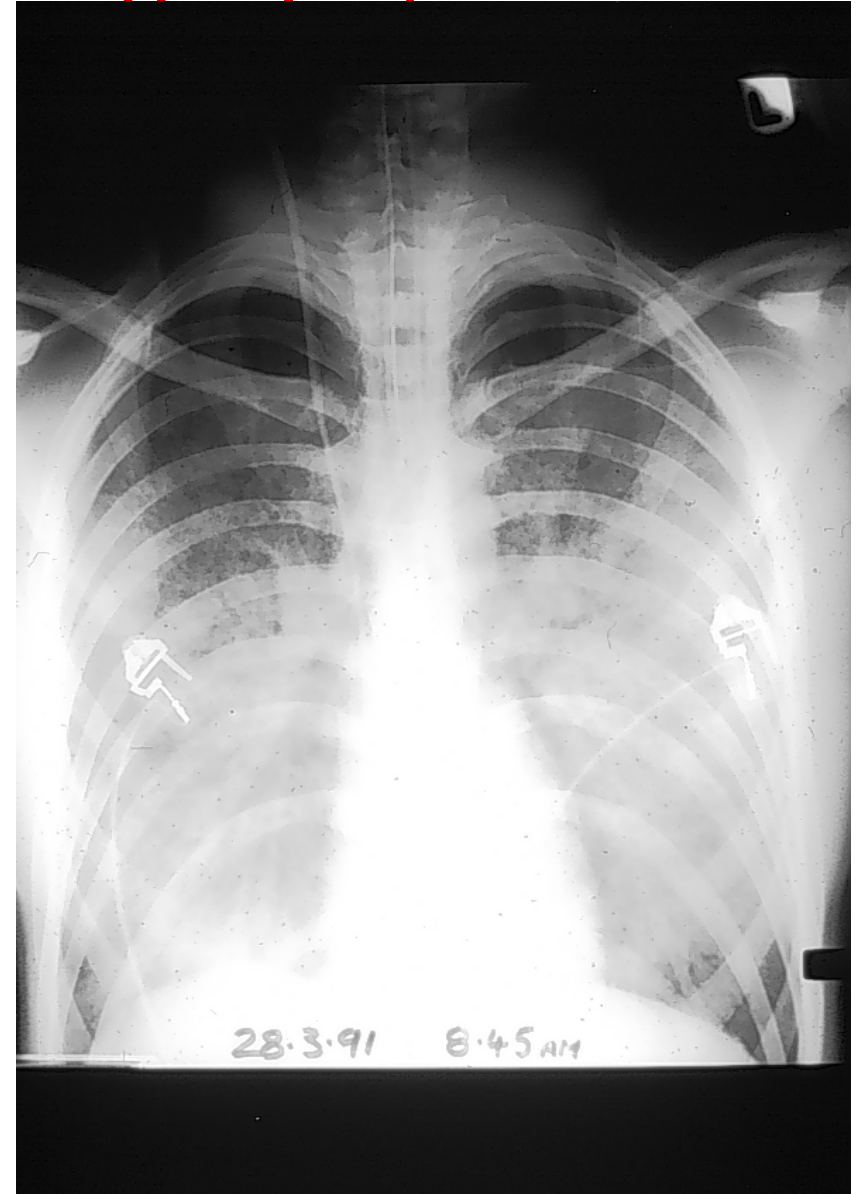


# Using SHOT data to prevent transfusion-related acute lung injury

- Leading cause of mortality and major morbidity 1996-2003
- Caused by HLA/HNA antibodies
- Main source is donor plasma:



- Female donors with a history of pregnancy: antibodies in 10-15% (MacLennan & Navarrete)



# TRALI – relative risk from different components 1996-2003

|  | Red cells  | Cryo      | FFP       | Platelets |
|--|------------|-----------|-----------|-----------|
| TRALI cases  | 33         | 2         | 31        | 27        |
| Components issued                                  | 18,370,000 | 634,000   | 2,515,000 | 1,842,000 |
| Risk/<br>component issued                          | 1:556,000  | 1:317,000 | 1:81,000  | 1:68 000  |
| <b>Relative risk<br/>compared to red<br/>cells</b> | <b>1</b>   | <b>2</b>  | <b>7</b>  | <b>8</b>  |

# A simple, low cost intervention to reduce the risk of TRALI

**‘No more  
questions for  
donors please’**

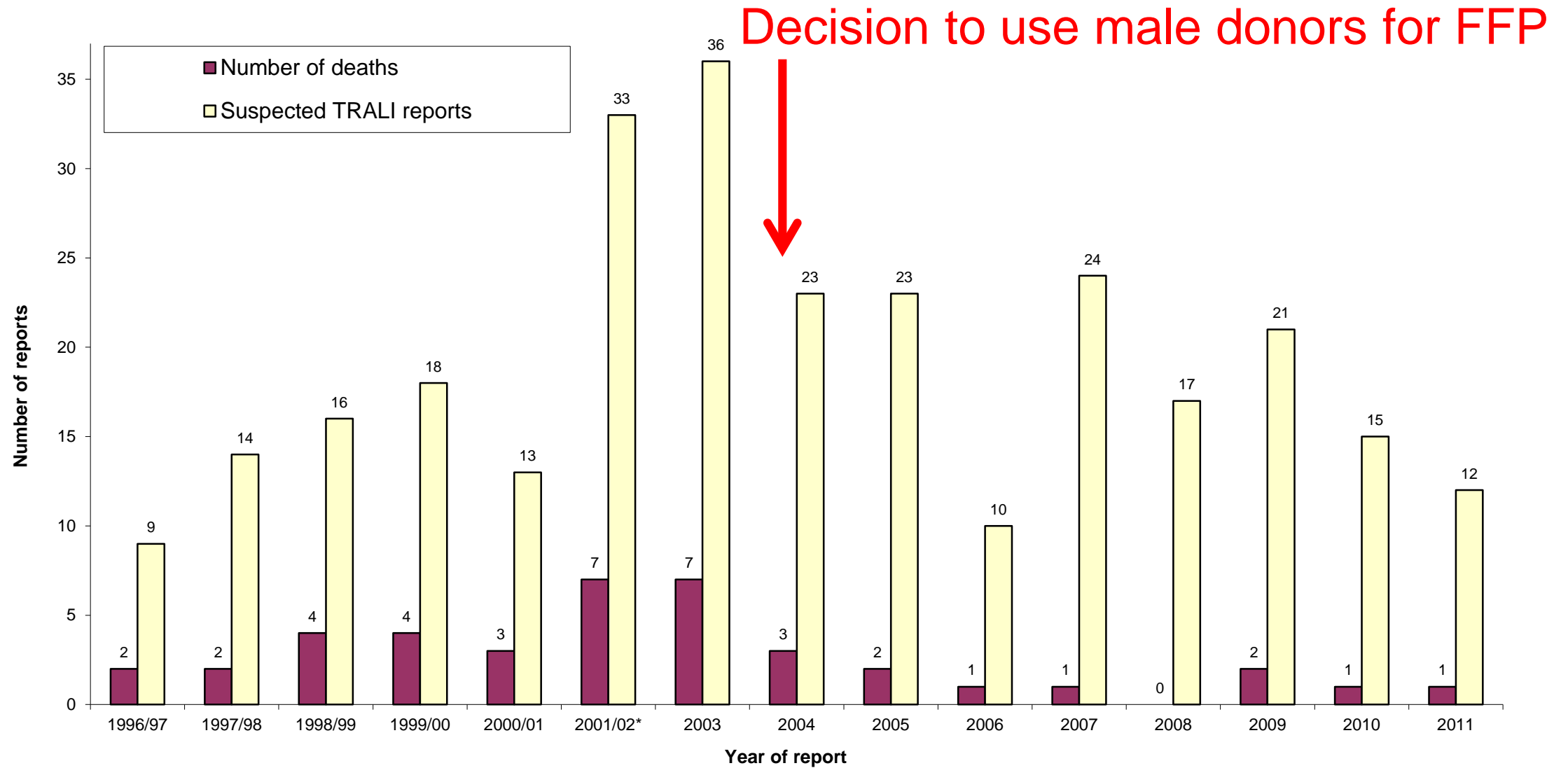


**October 2003:**

**Plasma packs marked M  
and F**

**M plasma for FFP**

**F plasma discarded**



Chapman CE, Stainsby D, Jones H, Love E, Massey E, Win N, Navarrete C, Lucas G, Soni N, Morgan C, Choo L, Cohen H, Williamson LM; Serious Hazards of Transfusion Steering Group. Transfusion 2009; 49: 440-452.



# James Blundell 1790-1878



MD Edinburgh 1813

First transfusion 1828

N = 10 transfusions in total  
(80 years before blood groups!)  
Success rate = 50%





# **1992: RCT of Pall bedside leucoreduction filters in preventing HLA alloimmunisation in haematology patients**

**LW to NBS  
Cambridge Issue  
Department:  
'Please send a  
box of Pall filters  
to Kings Lynn  
blood bank'.**



# **RCT of Pall bedside leucoreduction filters in preventing HLA alloimmunisation**

**Kings Lynn Blood Bank to LW:  
‘Why have you sent us these oil filters for car engines?’**



**3. Avoid  
words with  
more than one  
meaning**



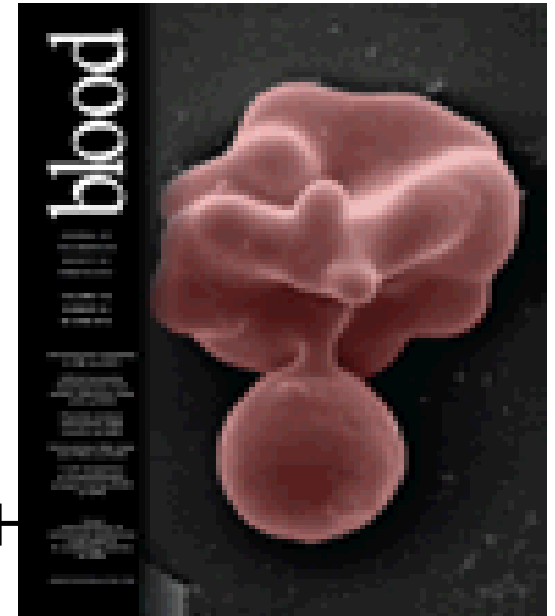


# RCT of Pall bedside leucoreduction filters in preventing HLA alloimmunisation: Conclusions

1. Bedside post-storage leucoreduction does not prevent HLA alloimmunisation

2. Negative trials can get into good journals if the question is important

(Williamson LM, Wimperis JZ, Williamson P, Copplestone JA, Gooi H, Morgenstern GR, Norfolk DR. Blood 1994;10:3018-3025)



3. 'Marcela, we need a clinical trials unit'- Williamson & Murphy 1998












[www.nhsbt.nhs.uk/clinical-trials-unit](http://www.nhsbt.nhs.uk/clinical-trials-unit)

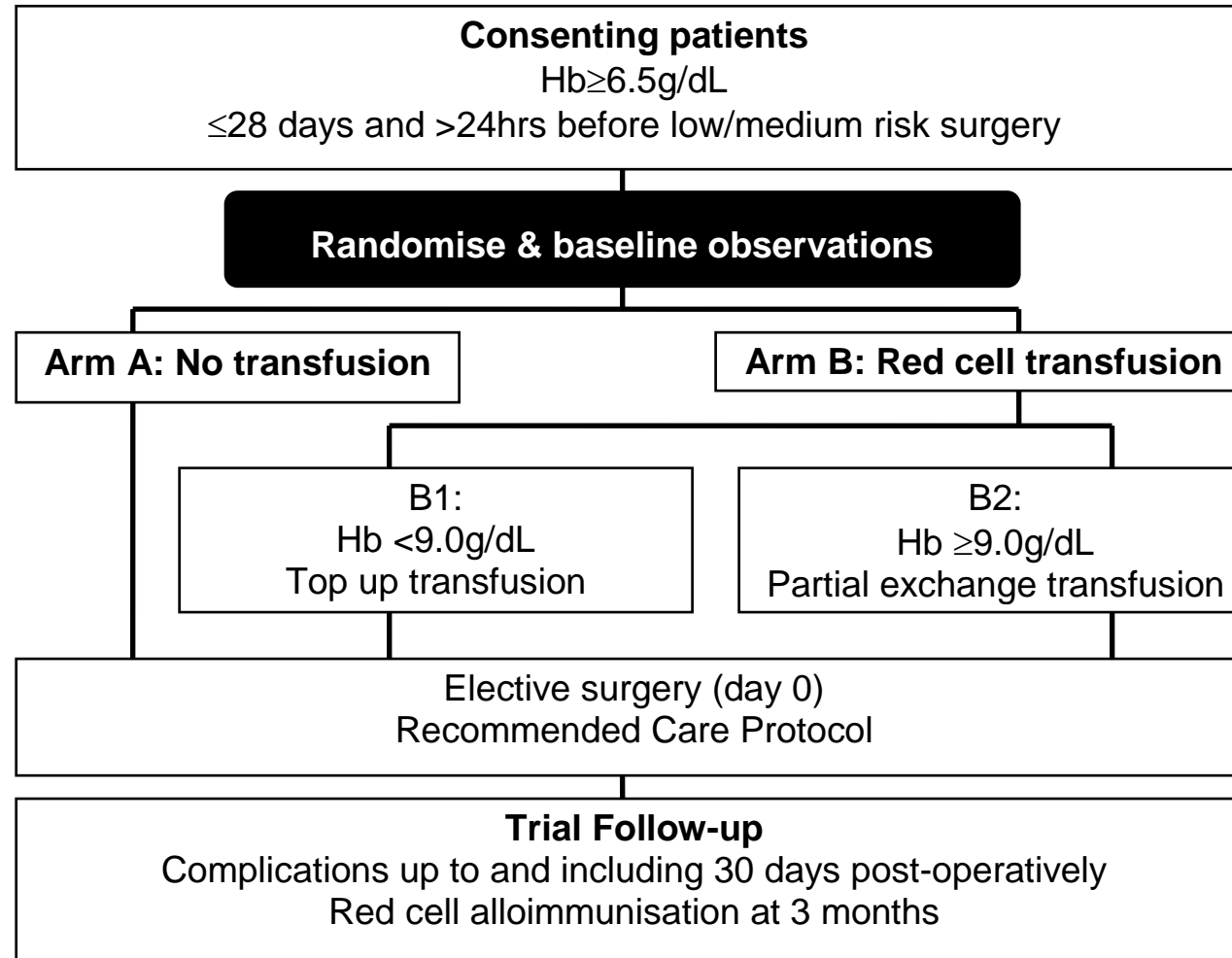


# CTU: Current activity

## 13 studies incl 3 of organs

|   |  |
|---|--|
| <b>PlaNeT-2</b>   | A randomised controlled trial to compare two different platelet count thresholds for prophylactic platelet transfusion to preterm neonates   |
|                  | A comparison of HLA epitope-matched with standard HLA-matched prophylactic platelet transfusions in raising the platelet count increment in alloimmunised thrombocytopenic patients with aplastic anaemia, myelodysplastic syndrome or acute myeloid leukaemia: a double-blind randomised cross-over trial |
|                  | A double blind, randomised controlled trial evaluating the safety and efficacy of tranexamic acid in patients with haematological malignancies with severe thrombocytopenia  |
|                  | A multi-centre, randomised, double blind, placebo controlled trial evaluating the effects of early administration of fibrinogen concentrate in adults with major traumatic haemorrhage   |
| <b>REDDS</b>  | Red blood cell transfusion thresholds and QoL in myelodysplastic syndromes: a pilot, feasibility study   |
| <b>EVNP</b>   | A multicentre, randomised, open label trial comparing graft function and survival following transplant of kidneys preserved using cold storage alone vs cold storage plus 1 hour normothermic perfusion. Collaboration with University of Cambridge  |
|                  | A placebo-controlled single-blind, randomised feasibility trial of Desmopressin (DDAVP) in critical illness prior to procedures  |
|                  | A cross-over trial comparing recovery and survival of manufactured RBCs with standard donated RBCs in healthy volunteers   |
| <b>REAL</b>   | A feasibility cross-over randomised controlled trial comparing restrictive versus liberal red cell transfusion strategies in adult patients with acute myeloid leukaemia receiving intensive chemotherapy  |
| <b>REPAST</b>   | A feasibility randomised controlled trial comparing restrictive versus liberal red cell transfusion strategies in children undergoing allogeneic haematopoietic stem cell transplant (HSCT)  |
| <b>REDJUVENATE</b>  | Feasibility trial of Rejuvesol, RBC rejuvenating solution, in patients undergoing cardiac surgery. Collaboration with University of Leicester.   |
| <b>CRYO-STAT-2</b><br><small>EARLY CRYOPRECIPITATE IN TRAUMA</small>                              | A multi-centre, randomised, controlled trial evaluating the effects of early administration of cryoprecipitate in adults with major traumatic haemorrhage. Collaboration with Barts and The London Hospital.   |
| <b>ITOPS</b>  | Improving Transplant Opportunities for Patients who are Sensitised (ITOPS) – a pilot, open label, randomised, controlled phase III trial in kidney transplantation   |
| <b>ISOC-3</b>   | A pilot randomised trial of diagnostic strategies for acquired coagulopathy in critical care and Core Outcome Set development  |
| <b>PITHIA</b>  | Pre-Implantation trial evaluating the effect of providing an urgent Histopathology result service on the rate of transplantation of kidneys from donors aged over 60 years.  |

# 2007 TAPS RCT: Does pre-operative transfusion in sickle cell disease increase or decrease the overall incidence of significant peri-operative complications?





# TAPS Trial progress

- Nov 2007: Trial opened
- Sept 2010: 1<sup>st</sup> interim analysis (n = 40)
  - An imbalance in patients with Serious Adverse Events was noted
- Feb 2011: (n = 70 enrolled)
  - Imbalance in patients with SAEs more marked
  - Data Monitoring Committee request unscheduled interim analysis (n = 61)

# TAPS: Primary Outcome and Serious Adverse Events (SAEs)

| Trial Arm                                  | Arm A –<br>No Pre-operative<br>blood transfusion | Arm B –<br>Pre-operative<br>blood transfusion | Overall   |
|--|--|---|---|
| Patients Recruited                         | 33   | 34  | 67  |
| Patients with significant<br>complications | 13 (39.3%)                                       | 5 (14.7%)                                     | 18 (26.9%)<br>OR 3.8 (CI 1.2-12.2)<br>p 0.027               |
| Patients with SAEs                         | 10 (30.3%)                                       | 1 (2.9%)                                      | 11 (16.4%)<br>27.4% difference<br>(CI 10.6-44.0)<br>P 0.003 |
| Patients with Acute Chest<br>Syndrome      | 9 (27.3%)  | 1 (2.9%)                                      | 10 (14.9%)  |

# TAPS: the only way is ethics

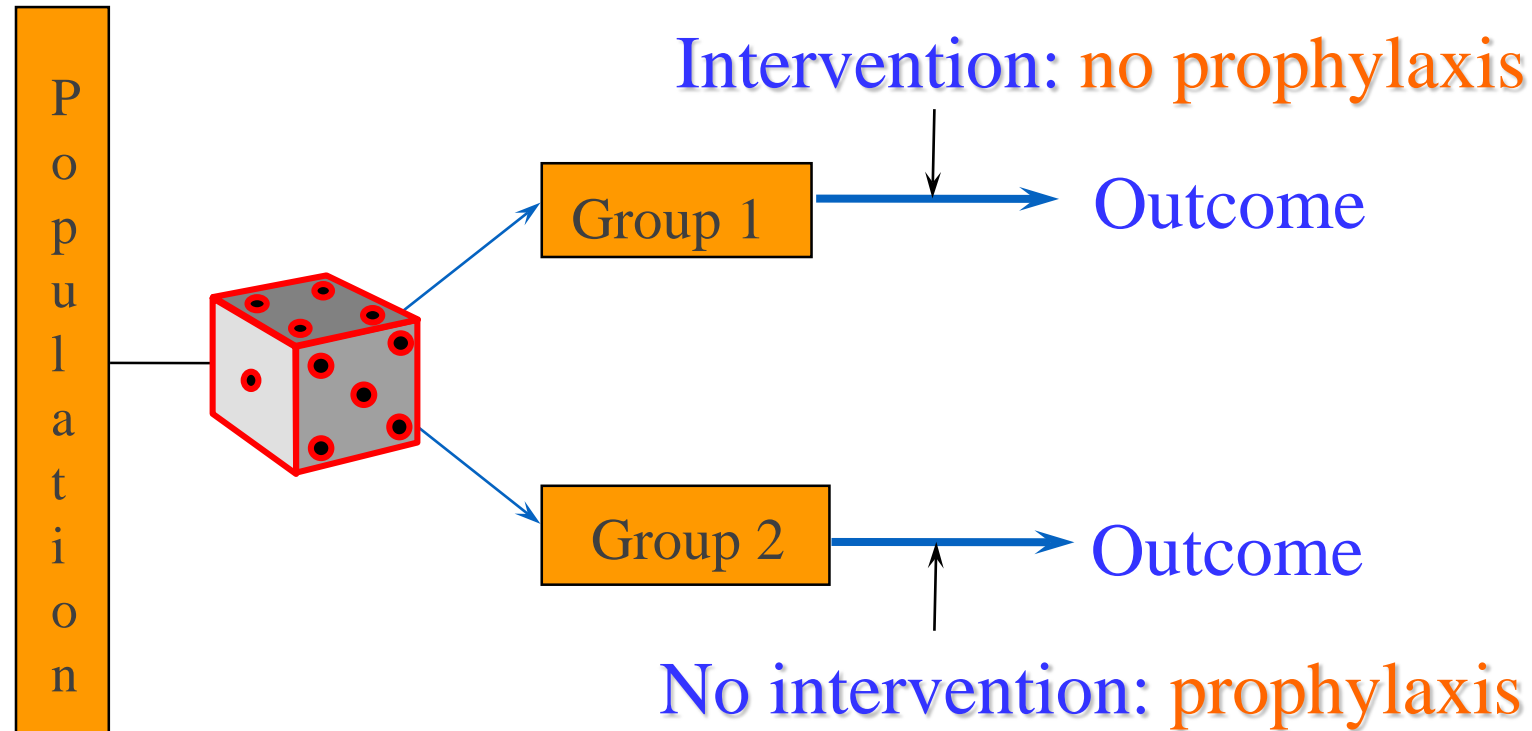
- Trial Steering Committee closed TAPS early in March 2011
- **Conclusion: Pre-operative transfusion should be offered to patients with HbSS having medium risk surgery and be considered in other genotypes and in low risk surgery**
- Trials confirming current practice are still important

Howard J, Malfroy M, Llewelyn C, Choo L, Hodge R, Johnson T, Purolit S, Rees DC, Tillyer L, Walker I, Fijnvandraat K, Kirby-Allen M, Davies SC, Williamson LM.

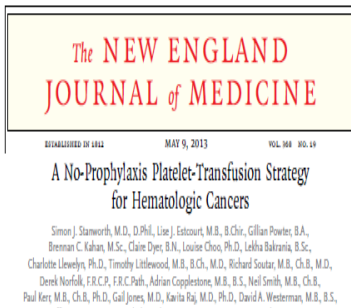
Lancet 2013; 381:930.

## 4. Pictures can be helpful----

# TOPPS: Trial of platelet prophylaxis vs no prophylaxis



Stanworth et al  
NEJM  
9<sup>th</sup> May 2013

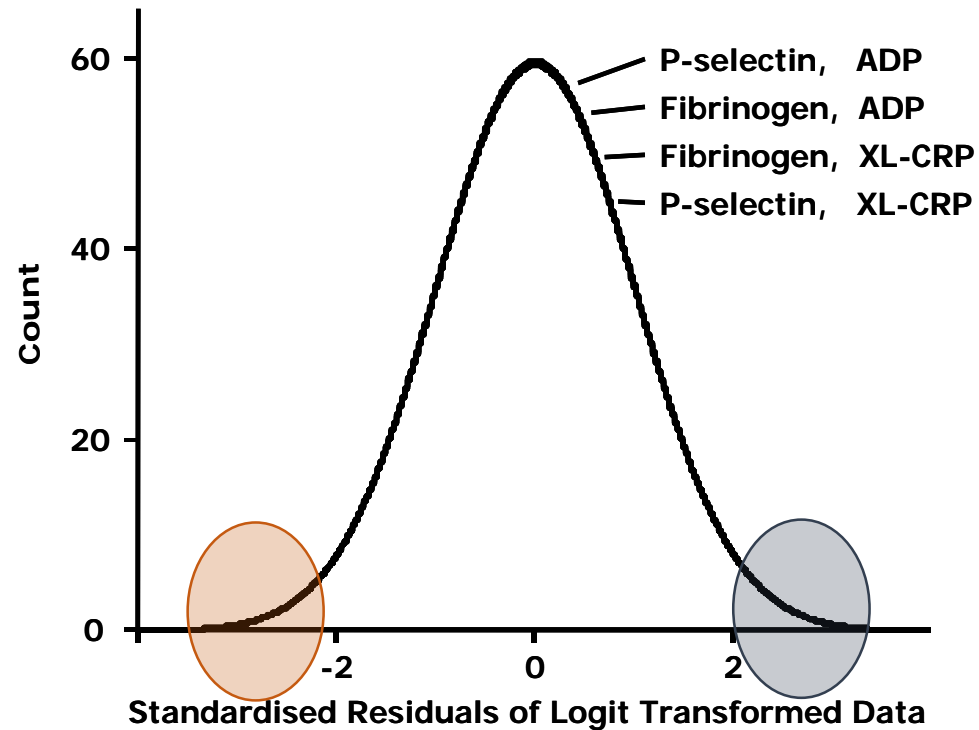


----but not  
always.

(guess  
which Royal  
College)



# PROMPT RCT: Do differences in donor platelet function in lab tests affect patient outcomes after platelet transfusion?

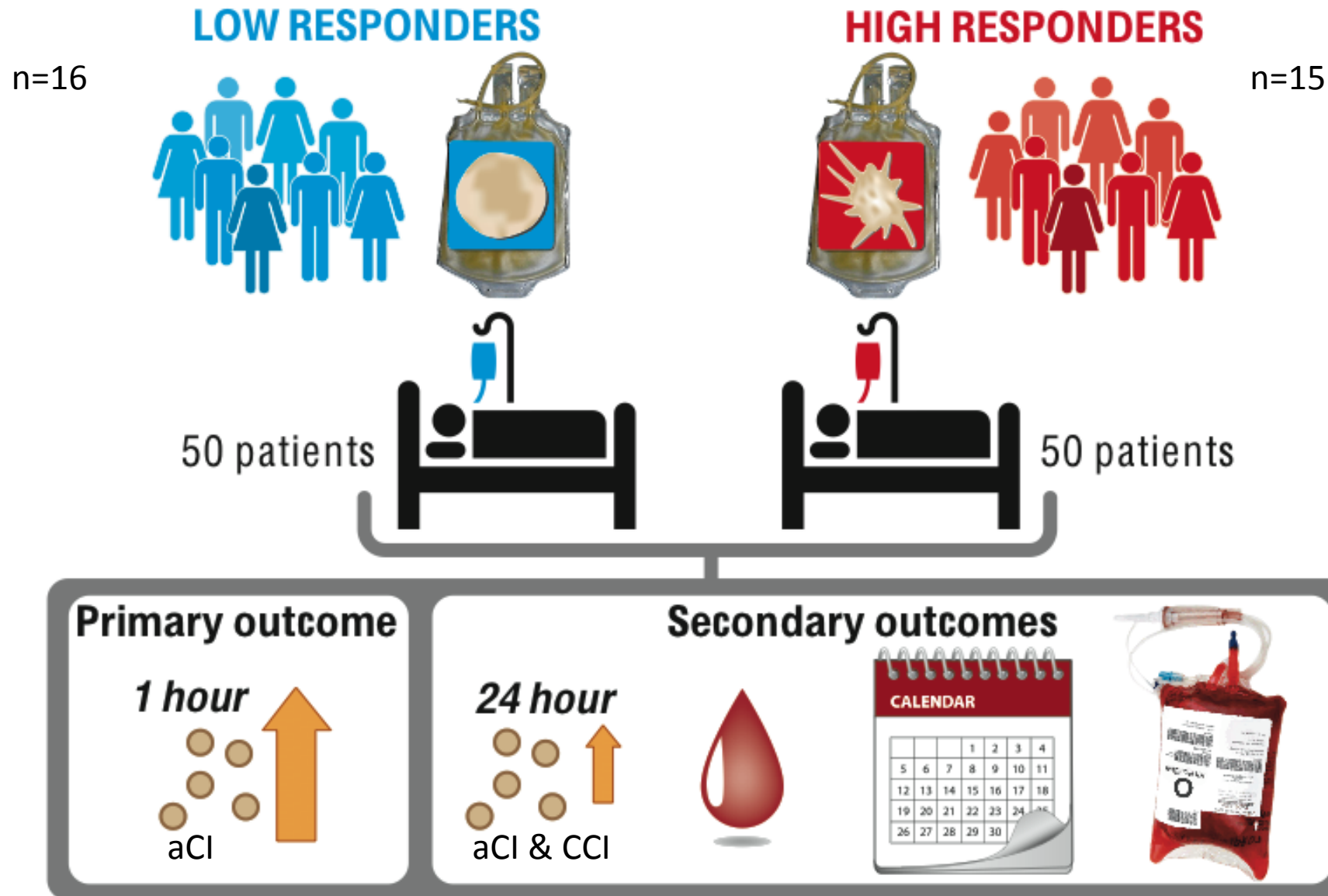


≠  
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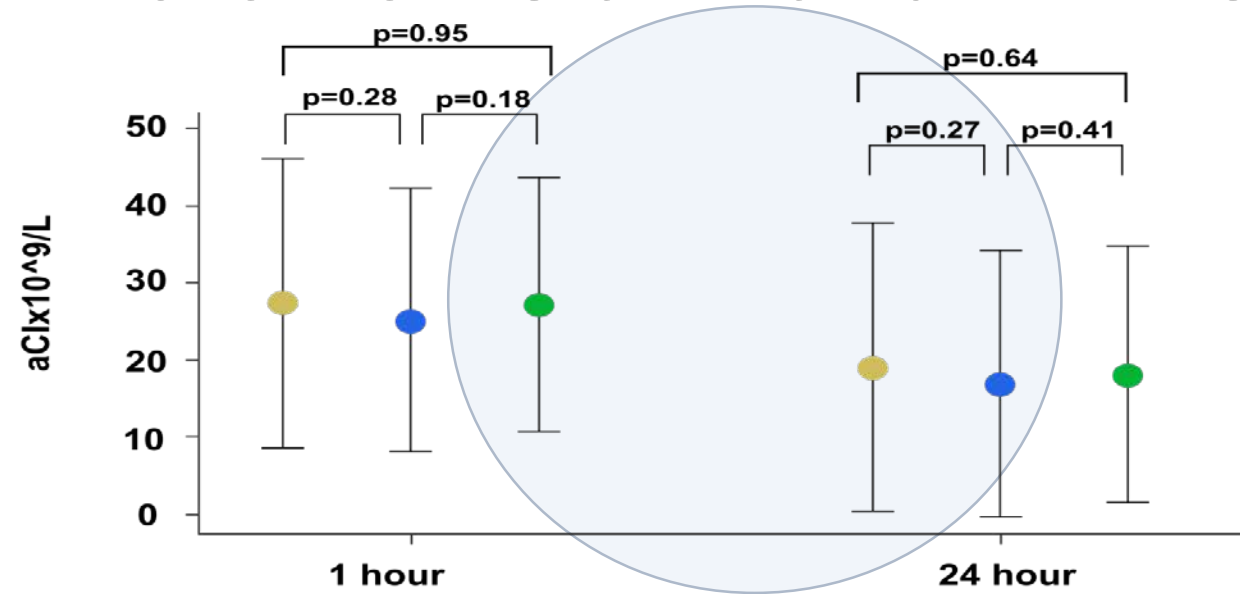


Cambridge Platelet Function Cohort – n=506  
Jones et al. JTH 2007; 1756-1765

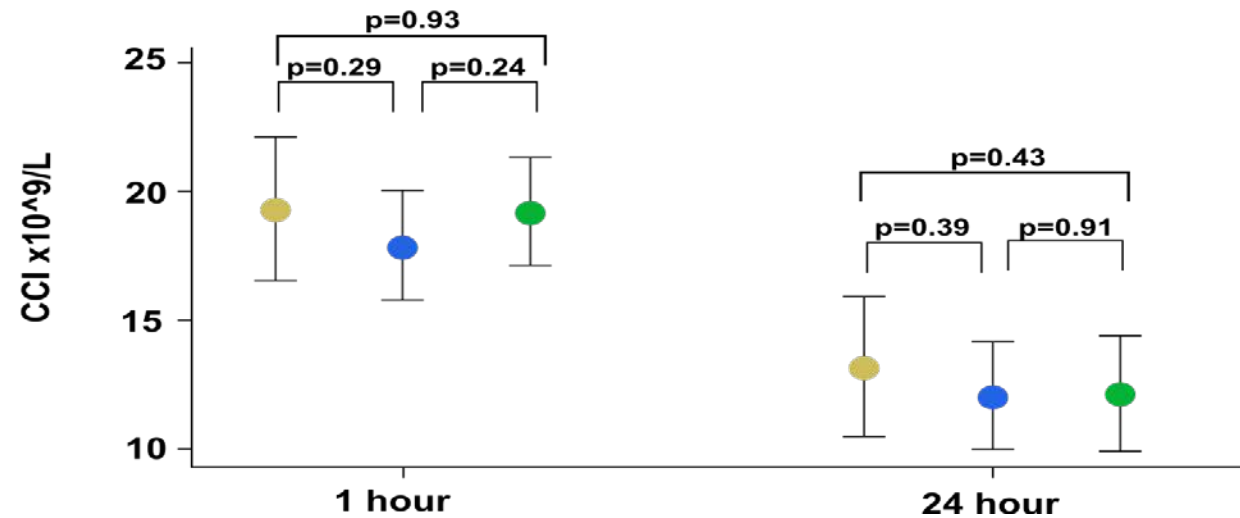
# Platelet Responsiveness and Outcome from Platelet Transfusion (PROMPT)



# PROMPT results – platelet count increments at 1 and 24 hrs



● Unselected  
● High responder  
● Low Responder





# PROMPT: Conclusions

- Differences in donor platelet responsiveness do not affect count increments, bleeding scores or component usage in recipients of prophylactic platelets
- Might patients who are actively bleeding benefit from PC from a high responder donor?
- 'Negative' trials, if well performed, can still get into top journals
- Clinical fellows are worth their weight in gold- so are clinical scientists

Kelly AM, Gardner SF, Foukaneli T, Godec TR, Herbert N, Kahan BC, Deary A, Bakrania L, Llewelyn C, Ouwehand WH, Williamson LM, Cardigan RA. Blood 2017;130:214

## 5. The Great British Fake Off

Red blood cells  
and plasma  
made to GCP  
(Good Culinary  
Practice)



## 6. Adults love 'Make & Take'.

Antigens,  
antibodies and  
leucocytes





**Science  
Museum  
Lates for  
adults:**

**Making  
antibodies to  
viruses**



## 7. Get them young



**Pathology Summer School for undergraduates**



--and younger--





# Schools Science Conference





----and even  
younger----

**Clotting,  
transfusion and  
blood groups:  
Bellbird Primary  
School Science  
Club,  
Sawston**





**8. Link  
science and  
art  
RCPATH Art  
Competition**

**‘Animals in  
pathology’**

**Under 8s  
winner**



**Hoarding,  
new RCPATH  
building site, Alie  
Street, Aldgate.**

**Thanks to English  
Catholic Martyrs  
Primary School  
and Dr Lizzie  
Burns.**







"I learn  
to use my  
imagination"

(year 4)

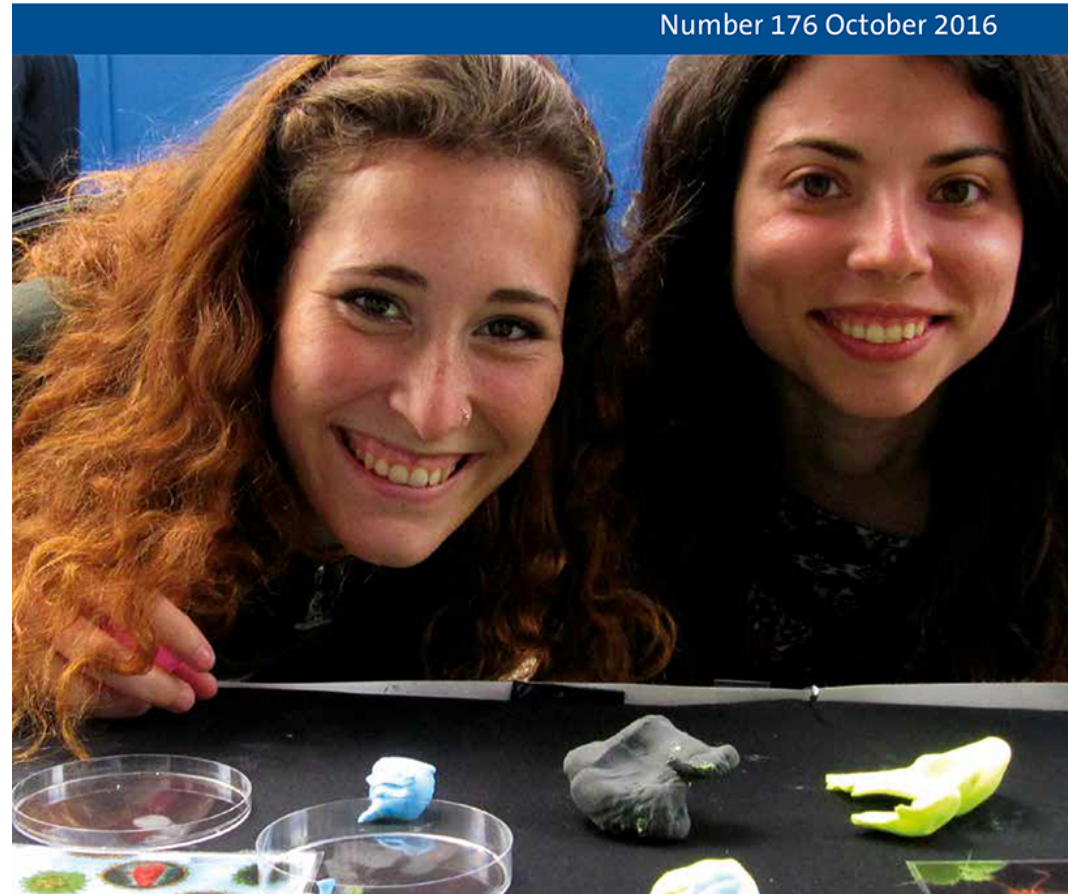
"It was  
wonderful  
learning about  
science"

(year 2)

# *The* Bulletin

of The Royal College of Pathologists

## Making bugs at the Oxford Science Festival 2016 with Dr Lizzie Burns



**9. Use  
animals.**

**Transfusion  
from the  
canine blood  
bank.**







**10. Hook up with celebrities in unusual places  
Low Allergy Garden, Chelsea Flower Show  
Which is RCPATH President and which is Lynda Snell ?**

# Thanks to many friends & colleagues!



Willem  
Ouwehand



Jean-Pierre  
Allain



Rebecca  
Cardigan



Cedric  
Ghaevert



Nick  
Watkins



Marcela Contreras



Sheila MacLennan



Mike Murphy