NHS Blood and Transplant

vCJD Interventions
How did we get here?

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Content

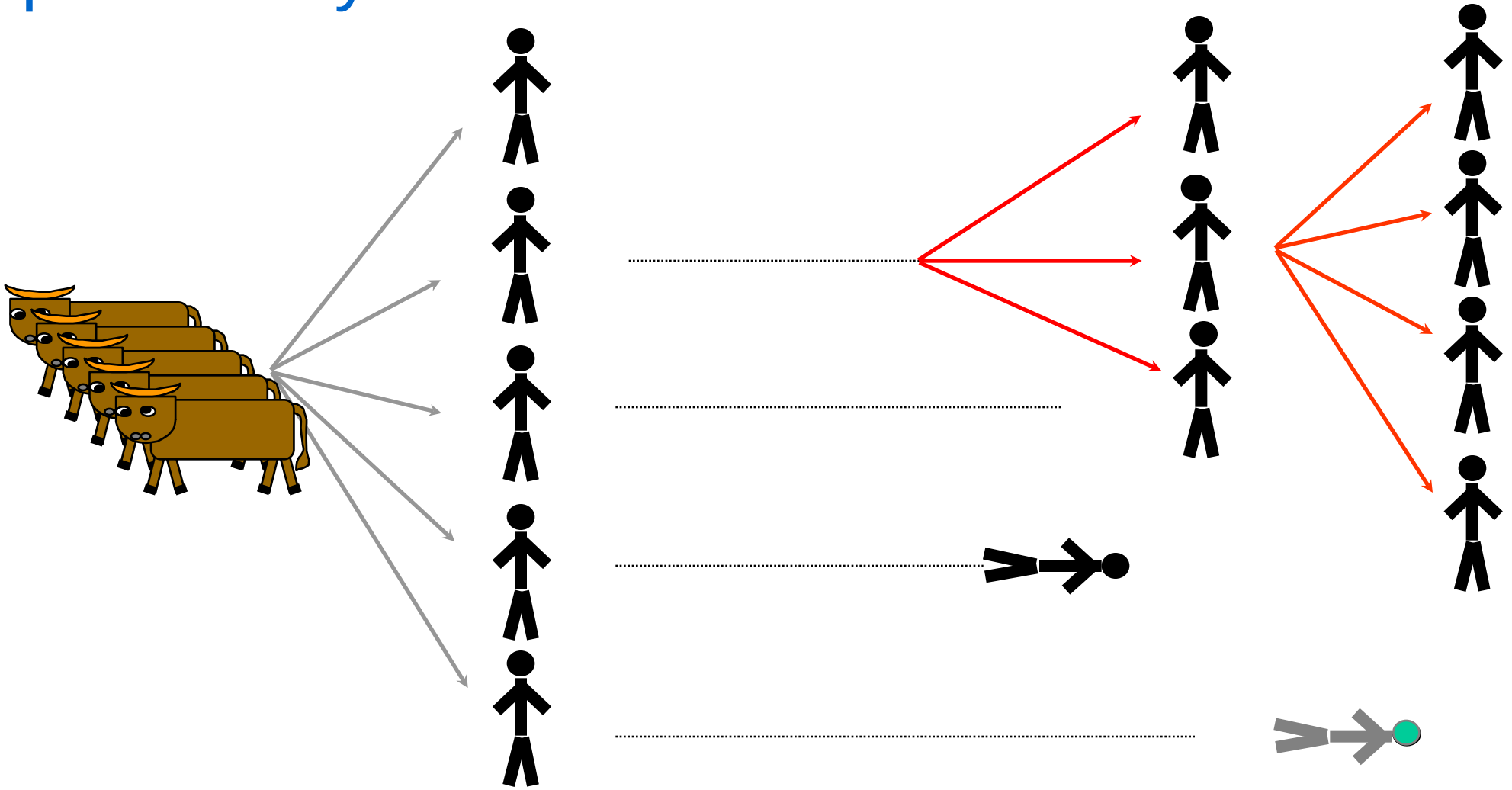
NHS Blood and Transplant

- vCJD and blood transfusion
- The role of SaBTO
- Current interventions
- New modelling
- What next?

Disclaimer: Only personal views being expressed

Potential expansion of vCJD epidemic by transfusion

(after Mike Busch)



BSE (<1996?)

infection (1/2000 – 1/40000)

incubation (5-40 years)

death

Transmission

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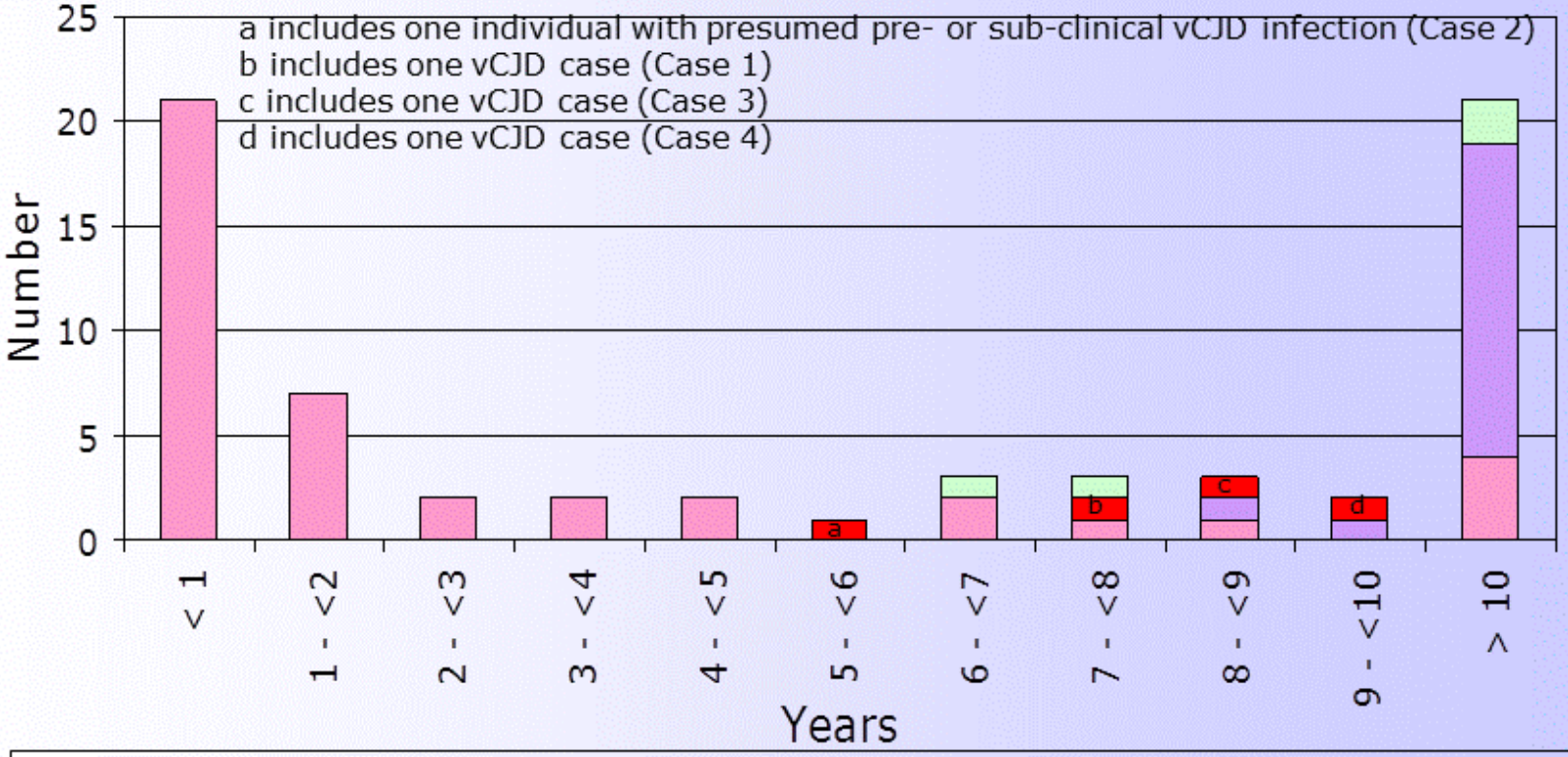
Number of vCJD cases in the UK	176
Number who were eligible to donate (ie aged 17 and over)	166
Number reported by relatives to have been blood donors	31
Number of cases where donor records have been traced	24
Number of cases from whom components were actually issued	18
Number of recipients identified from 18 cases where recipient and component information is available	67

http://www.cjd.ed.ac.uk/

RECIPIENTS OF LABILE BLOOD COMPONENTS DONATED BY vCJD CASES (n=67)



DEAD (n=50)

- Dead - untested
- Dead - tested positive for PrP deposition
- Dead - tested negative for PrP deposition

(Interval from transfusion to death)

ALIVE (n=17)

- Alive - untested
- Alive - tested for PrP deposition

(Interval from transfusion to Sept 2012)

http://www.cjd.ed.ac.uk/

Diagnoses

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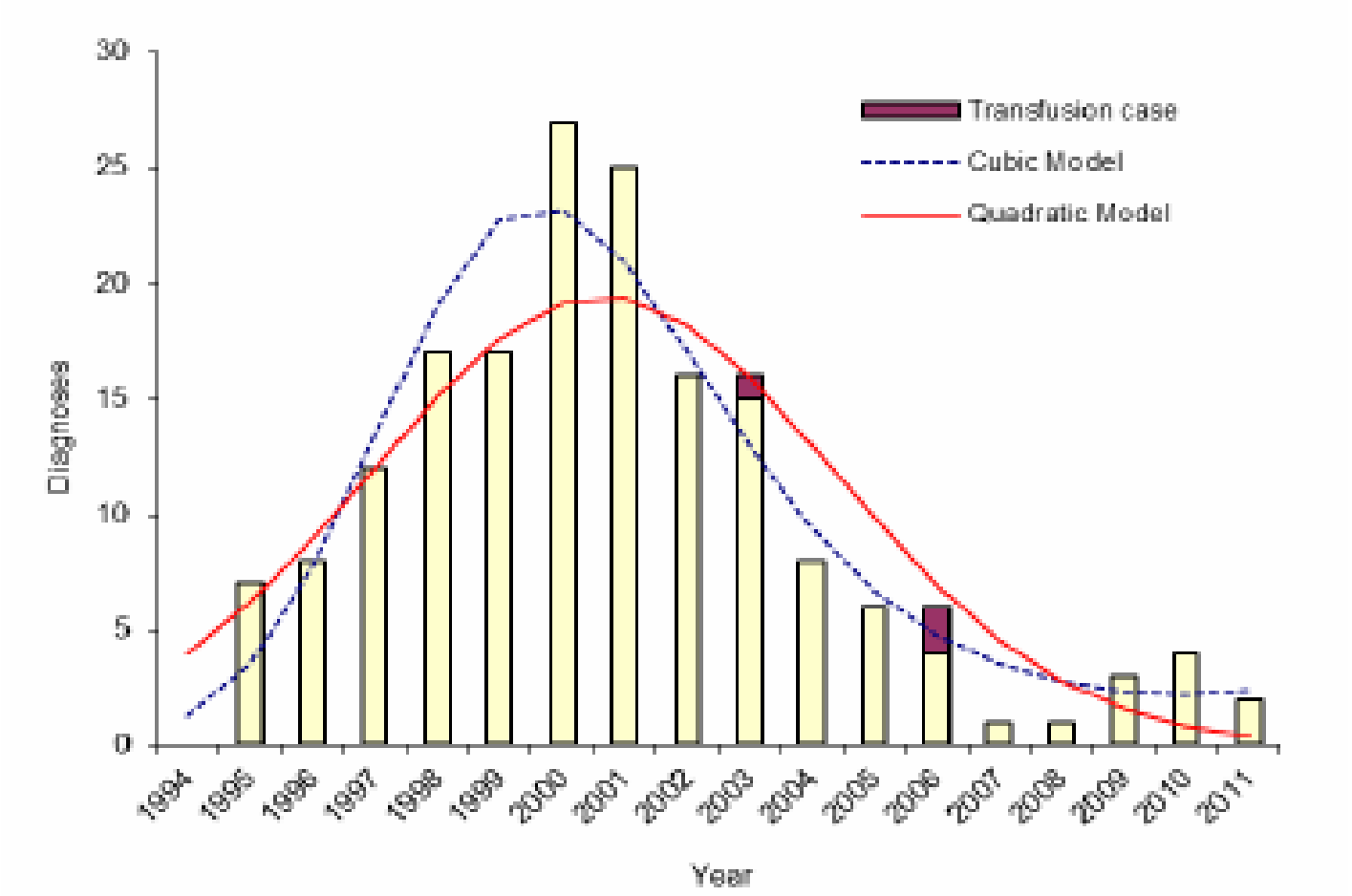
NJ Andrews, HPA
http://www.cjd.ed.ac.uk/



SaBTO

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- Independent Advisory Committee on the Safety of Blood, Tissues and Organs
- Terms of reference include:
  - take into account sufficiency of supply and quality
  - consider the efficacy of transfusion
  - consider the cost-effectiveness of interventions
  - interpret risk assessments (eg by ACDP)
  - take full account of scientific uncertainty and assumptions
- Makes recommendations to UK governments

www.dh.gov.uk/health/about-us/public-bodies-2/advisory-bodies/sabto

Governments of the UK

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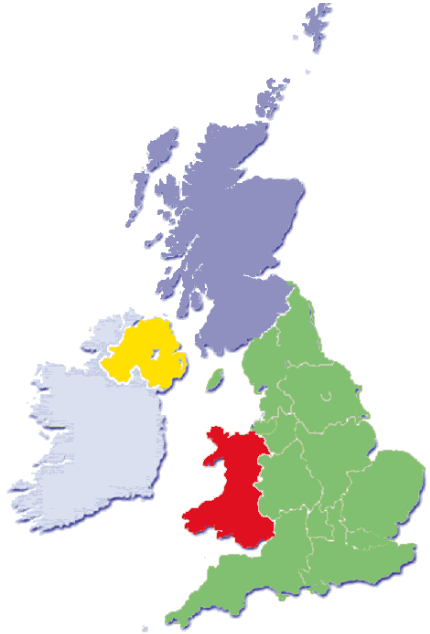
UK Government

- Scottish Government
- Northern Ireland Executive
- Welsh Assembly Government
- No devolved equivalent for England



- Each with its own Department of Health
- Decision makers (± Ministerial approval)

Current interventions

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- UK plasma not used for fractionation
  - since 1997
- LD all blood components
  - since 1999
- exclude donors transfused after 1980
  - since 2004
- import FFP from BSE free countries for those born >1st Jan 1996
  - since 2004, extended to all <16 years 2005
  - amended to those born on/after 1.1.96 (2012)

Platelets

- Jan 04
  - A phased increase in platelet procurement by apheresis
  - Single donor v 4 donors per component
- July 09
  - UK Blood Services should:
    - move as far as possible towards 100% apheresis
    - minimum of 80% of platelets should be apheresis

What's new?

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- Mis-match of previous modelling with clinical cases
- New publications on infectivity and epidemiology

→ Need to revisit and revise the scenarios

Defining the risk

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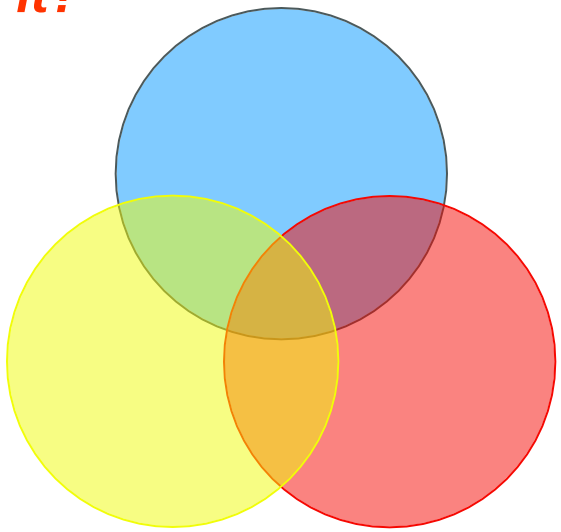
Prevalence

How many people have it?



Infectivity

How infectious are they?

Susceptibility

Who could catch it?

Modelling

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- By DH Health Protection Analytical Team
  - Peter Bennett and Maren Daraktchiev
  - DH analysis has been developed with help from CORU
  - Publication of latest Imperial College model (Ghani & Garske)
- TSE Risk assessment sub group

  of the Advisory Committee on Dangerous Pathogens (ACDP)

Previous scenarios

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- Used “High” and “Low” inputs for prevalence, infectivity and susceptibility.
- Prevalence (Infectious donors): *low* = 1 in 20,000; *high* = 1 in 4,000
  - Source: Hilton et al tissue survey (central estimate and lower 95% CI)
  - Applied to all cohorts exposed to the BSE outbreak.
- Infectivity (whole blood): *low* = 0.1 i.v.ID/ml; *high* = 30 ID/ml.
  - Many IDs per unit (~ 300 ml)
  - White cells (leucocytes) and plasma, in roughly equal proportions.
  - Source: SEAC, rodent models
- Recipients susceptible to clinical vCJD: *low* =10%; *high* = 100%
  - 100% is the precautionary assumption. Lack of evidence for any lower figure, but 10% similar to a hypothesis to explain the modest number of primary cases (Clarke and Ghani, 2005).
  - Allows a long-term, possibly infectious, “carrier state”.

Eight Scenarios

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~400 cases

Prevalence

HIGH Susceptibility to clinical vCJD (100%)	1 in 4000 (1 in 4000); HIGH Infectivity (30 ID/ml)
	1 in 4000 (1 in 4000); LOW Infectivity (0.1 ID/ml)
	1 in 20000 (1 in 20000); HIGH Infectivity (30 ID/ml)
	1 in 20000 (1 in 20000); LOW Infectivity (0.1 ID/ml)
LOW Susceptibility to clinical vCJD (10%)	1 in 4000 (1 in 4000); HIGH Infectivity (30 ID/ml)
	1 in 4000 (1 in 4000); LOW Infectivity (0.1 ID/ml)
	1 in 20000 (1 in 20000); HIGH Infectivity (30 ID/ml)
	1 in 20000 (1 in 20000); LOW Infectivity (0.1 ID/ml)

In isolation, all three inputs make sense, but together they don't match with observations (clinical cases)

New modelling

- Prevalence (Infectious donors)
  - Latest HPA data = 1 in 2000, within the limits used in the new model
  - www.hpa.org.uk/hpr/infections/ei_cjd.htm#cjd
- Infectivity (whole blood)
  - Based on human transmissions, only 0.3 – 0.75 ID per **unit**
  - Source: Gregori et al
- Susceptibility to clinical vCJD
  - No new evidence, but no new UK cases for 2 years

→ Calibration of these variables to match the inputs with clinical data

Need to review…

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- Importation of FFP
  - For under 16s since 2004
  - 2009 recommendation to extend to all
  - Revisited by SaBTO, March 2012
- Red cell filtration
  - Recommendation for under 16s and haemoglobinopathies (2009)

→ HPAT papers - Andrew Parker and Peter Bennett

FFP cost-effectiveness

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- Estimate:
  - number of vCJD clinical cases resulting from FFP-borne transmission post-2012
  - number of vCJD symptom-free life-years lost
  - Subtract those in children or TTP patients (still to receive imported)

Table 4: Estimated number of vCJD symptom-free life-years lost resulting from FFP-borne transmissions to adult TTP patients after 2012, and remaining life-years to be saved by extending importation

	Scenario for preventable cases		
Symptom-free life years	**Lower bound**	**Central estimate**	**Upper bound**
No import			
Saved by import for children			
Saved by import for TTP patients			
Remaining			

~0.26M units in 20y

~5M units in 20y

"Importation of fresh frozen plasma, effectiveness and cost-effectiveness"
http://transparency.dh.gov.uk/2012/04/24/sabto-9-march-2012/

FFP cost-effectiveness

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- Calculate:
  - Number of units needed (20y) x cost of units
  - Divide by vCJD symptom-free life-years
- Commercially confidential results, but:
  - “the cost per life-year saved falls well above the normal threshold of £25,000, even in the most “generous” scenario for the number of cases prevented.”
  - “Although we are not reviewing the decision to import FFP for children...there are options where the cost ...is either below, or close to, the £25,000”

FFP reverse calculation

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- "the **maximum extra** cost at which extended importation would meet the normal cost-effectiveness criterion of £25,000 per symptom-free life year gained."

Table 7: Maximum Costs (£ per unit) meeting standard cost-effectiveness threshold

	Scenario for preventable cases		
	Lower bound	**Central estimate**	**Upper bound**
Maximum price per unit			

Red cell filtration

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SaBTO minutes of 9/3/12:

- "In October 2009, SaBTO had recommended that: "filtration of red cells be implemented, for those not exposed to BSE through diet (ie those born after 1996)."
- "implementation of prion filtration was dependent on the satisfactory completion of the PRISM study A"
- "The option to remove this measure should be exercised in the event of:

  (i) further data on prevalence or

  (ii) filters proven to not be efficacious when used widely;

  and that this recommendation will be kept under review as further data emerges on prevalence, infectivity and susceptibility and the efficacy of the filters."

Red cell filtration

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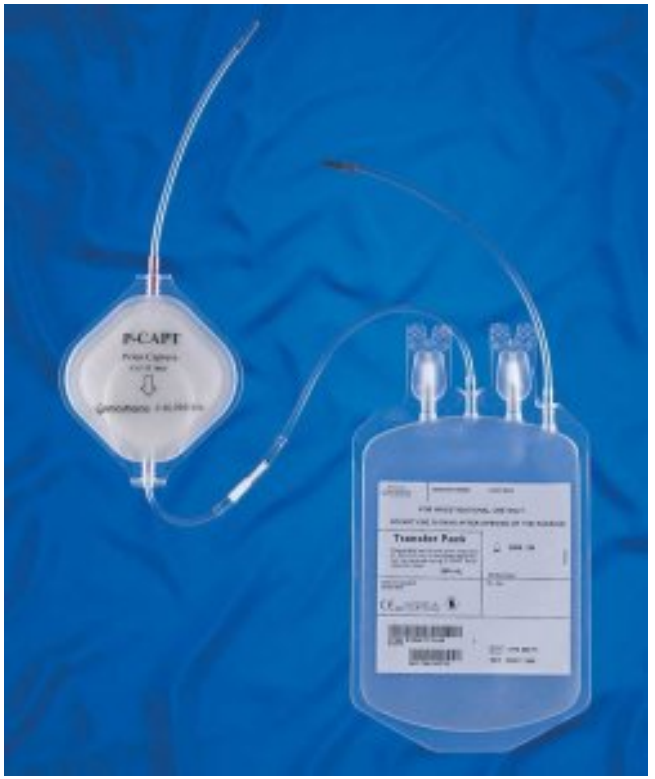
- PRISM A is complete, and SaBTO accepted:

  i) that the use of the filter did not reduce the overall safety of transfusion.

  ii) if implemented... would require post-marketing surveillance to assess continued safety in large populations of transfused patients.
- "The efficacy evidence in 2009 was largely based on spiked brain homogenate... this does not reflect potential natural infectivity in whole blood, and it was therefore crucial to have the results of the studies of the efficacy ... under way in hamsters and sheep using endogenous blood infectivity."



Red cell filtration

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SaBTO minutes of 9/3/12:

- "SaBTO put on hold its recommendation of 2009, pending

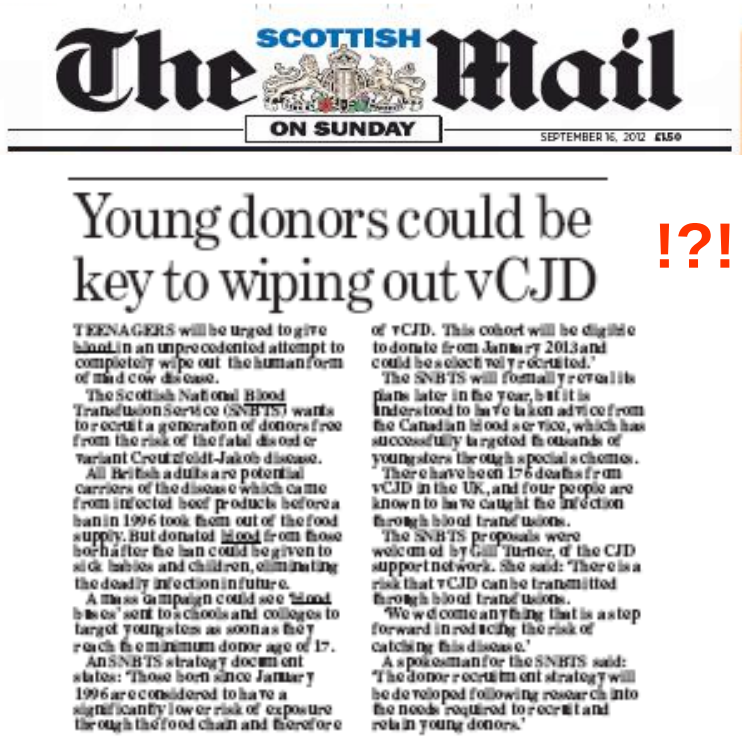
  a) the completed current prevalence IHC study of stored appendix tissue;

  b) the final report of the independent evaluation of filter efficacy (hamster study at HPA); and

  c) additional preliminary data from the sheep study at Roslin (ie as available at the time that items (a) and (b) are available, but not awaiting completion of the study in 2014)"
- Anticipate a review in December 2012
  - same format as described for FFP given above
  - including a reverse calculation?

“Club 96”

- Born on/after 1 Jan 1996
- Likely to be less exposed to BSE in the food chain
- Appendix study proposed
- When can a sustainable supply be achieved?



SCOTTISH The Mail ON SUNDAY

SEPTEMBER 16, 2012 £1.50

Young donors could be key to wiping out vCJD

!?!

TEENAGERS will be urged to give blood in an unprecedented attempt to completely wipe out the human form of mad cow disease.

The Scottish National Blood Transfusion Service (SNBTS) wants to recruit a generation of donors free from the risk of the fatal disorder variant Creutzfeldt-Jakob disease.

All British adults are potential carriers of the disease which came from infected beef products before a ban in 1996 took them out of the food supply. But donated blood from those born after the ban could be given to sick babies and children, eliminating the deadly infection in future.

A mass campaign could see 'blood buses' sent to schools and colleges to target youngsters as soon as they reach the minimum donor age of 17.

An SNBTS strategy document states: 'Those born since January 1996 are considered to have a significantly lower risk of exposure through the food chain and therefore of vCJD. This cohort will be eligible to donate from January 2013 and could be selectively recruited.'

The SNBTS will formally reveal its plans later in the year, but it is understood to have taken advice from the Canadian blood service, which has successfully targeted thousands of youngsters through special schemes.

There have been 176 deaths from vCJD in the UK, and four people are known to have caught the infection through blood transfusions.

The SNBTS proposals were welcomed by Gill Turner, of the CJD support network. She said: 'There is a risk that vCJD can be transmitted through blood transfusions.

'We welcome anything that is a step forward in reducing the risk of catching this disease.'

A spokesman for the SNBTS said: 'The donor recruitment strategy will be developed following research into the needs required to recruit and retain young donors.'

What next?

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- Studies
  - Appendices of Pre-1980 and Post-1996?
  - Blood prevalence?
- Interventions
  - Other red cell filters PR+LD?
  - Review of 80% apheresis platelets?

Acknowledgments

- Department of Health
  - SaBTO Secretariat
  - Health Protection Analytical Team
- SaBTO
- National CJD Research and Surveillance Unit
- Health Protection Agency