The risk of vCJD transmission by blood components – SaBTO review of pooled versus apheresis platelets.

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Context

- In 2008 the Committee on the Microbiological Safety of Blood, Tissues and Organs (MSBTO) set a target of 80% platelet collection by apheresis as a vCJD risk reduction measure based on the working assumptions around prevalence, infectivity and susceptibility at that time.
- In 2009 the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) reviewed platelet risk reduction measures and upheld the recommendation to provide as many as possible by apheresis, but concluded that PAS offered no additional benefit because of the large amounts of infectivity estimated to be present in the associated plasma (<10ID / ml).

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Context

- In 2013 the working assumptions were revised by the Advisory Committee on Dangerous Pathogens (ACDP) TSE Risk Assessment Subgroup in light of further data on prevalence of subclinical infection and calibration of potential scenarios against the number of clinical cases of transfusion-transmitted vCJD actually seen to date.
- Specifically the point estimate for prevalence was increased from

  1 / 4,000 to 1 / 2,000 as a result of the Appendix II study (though this remains within the confidence limits of the previous working assumption).
- The infectivity point estimate fell from 5,000 ID to around 5 ID per unit of whole blood.

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Context

- In light of these changes in the working assumptions SaBTO was asked to review the relative effectiveness and cost-effectiveness of platelet apheresis and platelet additive solution as vCJD risk reduction measures.
- The assumptions relating to the number of potential cases of vCJD caused by platelet transfusion and the amount and distribution of infectivity in a platelet concentrate were reviewed by ACDP TSE RA subgroup.

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Apheresis vs pooled platelets – relative risk

Previous Assumptions

- Transmission certain from an infected donation.
- Majority of infectivity within the plasma, none in the platelets themselves.
- Apheresis:pooling risk 0.25.

Revised Assumptions

- Transmission no longer certain (esp. from the three donors per pool giving little plasma)
- Differential depends on assumed infectivity distribution between plasma and platelets
- Apheresis:pooling risk ratio

if all infectivity in plasma 0.57

Ratio increases if some infectivity in platelets

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Potential impact of additive solution

	Volume **mean (SD) mL/unit**	**Platelet yield mean (SD) x 10e9/unit**	**White Blood Cells mean (SD) x 10e6/unit**	**Plasma - current mean mL/unit**	**Plasma – in additive sol^{n} mean mL/unit**
Apheresis	198.8 (15.1)	292.2 (38.4)	0.41(13.8)	164	85
Pooled	298.0 (25.5)	316.5 (44.6)	0.34 (0.3)	241	85
Specification	N/A	> 240	< 5		

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Estimating potentially preventable cases

- Monte Carlo simulation was used to generate 30,000 scenarios to model the number of life years that may be saved by averting future cases through risk reduction measures under different assumptions around subclinical prevalence, infectivity and susceptibility.
- Only credible scenarios were used *i.e.* those where the prediction of clinical cases to date were consistent with reality (0-3 <2012).
- The effect of varying the proportion of infectivity in plasma and platelets and the proportion of platelets procured by apheresis was also modelled.

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Estimating potentially preventable cases

Future % Apheresis	Infectivity associated with platelets (IDs per whole blood donation)			
	0	**0.1**	**0.25**	**1**
80%	47 (1275)	50 (1381)	53 (1505)	63 (1830)
50%	56 (1518)	61 (1692)	68 (1914)	89 (2605)
35%	60 (1639)	66 (1848)	75 (2119)	103 (2993)
20%	65 (1761)	72 (2004)	82 (2323)	116 (3380)

Table assumes 3 IDs across platelets and plasma

Cases (and infections)

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Age Distribution of Donors

Apheresis donors tend to be older than whole blood donors

Appendix studies suggest higher prevalence among older donors

This reduces the potential benefit of apheresis.

Impact on potentially preventable cases (previous estimate):

Future % Apheresis	Infectivity associated with platelets (IDs per whole blood donation)			
	0	**0.1**	**0.25**	**1**
80%	67 (47)	72 (50)	77 (53)	91 (63)
50%	71 (56)	78 (61)	87 (68)	115 (89)
35%	72 (60)	80 (66)	90 (75)	123 (103)
20%	72 (65)	80 (72)	92 (82)	129 (116)

Table assumes 3 IDs across platelets and plasma

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Suspension in Additive Solution

Under previous infectivity assumptions, little impact on vCJD risk

Under revised infectivity assumptions, can have significant impact

Effectiveness of maintaining 80% apheresis with all units in plasma; compared to 80% pooled with all units in additive solution

IDs in Platelets (one whole blood donation)	IDs in Plasma (one whole blood donation)						
		1	1.5	2	3	4	5
	0						
	0.05						
	0.1						
	0.15						
	0.2						
	0.25						
	0.3						
	0.4						
	0.5						
	0.6						
	0.7						
	0.8						
	0.9						
	1						

Additive solution preferable

Depends on age differential

Apheresis preferable

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Suspension in Additive Solution

Suspension in additive solution is much cheaper than procuring platelets by apheresis

Cost-effectiveness of maintaining 80% apheresis with all units in plasma; compared to 80% pooled with all units in additive solution

IDs in Platelets (one whole blood donation)	IDs in Plasma (one whole blood donation)						
		1	1.5	2	3	4	5
	0						
	0.25						
	0.5						
	0.75						
	1						
	1.25						

Additive solution preferable

Depends on age differential

Apheresis preferable

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Estimated costs

We anticipate that most infections will take place over the next 20 years, and so calculate costs over this period.

Future Percentage of platelets collected by apheresis	Unit cost - pooled	Unit cost - apheresis	Total cost: all in plasma	Total cost: all in plasma (discounted)	Total cost: pooled in additive (discounted)	Total cost: all in additive (discounted)
80% apheresis	£34.79	£101.57	£506.4m	£372.4m	£378.8m	£404.3m
50% apheresis	£34.79	£103.85	£397.9m	£292.7m	£308.6m	£324.6m
35% apheresis	£34.79	£105.48	£341.8m	£251.4m	£272.1m	£283.2m
20% apheresis	£34.79	£107.18	£282.8m	£208.0m	£233.5m	£239.9m

Unit cost for suspension in additive solution: £7.55
Assume around 260k units issued per year, so around 5.74m produced in all (9.32% wastage)

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Cost-effectiveness (2)

- Use same infectivity scenario (0.25ID:2.75ID)
- First consider introducing additive solution with 80% procurement by apheresis

No age Differential

Future Percentage of platelets collected by apheresis	Production method	
	Pooled in additive	**Universal use of additive**
80% apheresis	£100k (£41k to £530k)	£300k (£120k to £1,500k)

Maximum Age Differential

Future Percentage of platelets collected by apheresis	Production method	
	Pooled in additive	**Universal use of additive**
80% apheresis	£72k (£29k to £360k)	£210k (£83k to £1,100k)

Normal cost-effectiveness threshold around £25k - £30k

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Cost-effectiveness (3)

No age Differential

Future Percentage of platelets collected by apheresis	Production method		
	All in plasma	**Pooled in additive**	**Universal use of additive**
50% apheresis	£400k (£160k to £2,000k)	£1,400k (£550k to £7,000k)	£2,600k (£1,000k to £13,000k)
35% apheresis	£400k (£160k to £2,100k)	£1,000k (£400k to £5,100k)	£1,100k (£440k to £5,600k)
20% apheresis	£410k (£160k to £2,100k)	£900k (£360k to £4,600k)	£930k (£370k to £4,700k)

Maximum Age Differential

Future Percentage of platelets collected by apheresis	Production method		
	All in plasma	**Pooled in additive**	**Universal use of additive**
50% apheresis	£590k (£240k to £3,000k)	-£1,000k (-£5,200k to -£410k)	-£490k (-£2,500k to -£200k)
35% apheresis	£690k (£270k to £3,500k)	-£1,600k (-£8,100k to -£640k)	-£1,000k (-£5,300k to -£410k)
20% apheresis	£810k (£320k to £4,100k)	-£1,900k (-£9,900k to -£780k)	-£1,600k (-£8,000k to -£630k)

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Summary

- Maintaining the proportion of platelet units procured by apheresis at 80% is not cost effective in any of the scenarios considered.
- Although the introduction of additive solution is not always cost-effective, it does always reduce the number of cases that we would expect.
- An overall package of reducing the level of apheresis and introducing additive solution is always more cost-effective than the current baseline.

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Recommendation and actions:

- SaBTO's recommendation: To remove the requirement to produce 80% of platelets by apheresis and that platelet additive solution should be used for the suspension of all platelets.
- In reality its is unlikely that UKBS will drop below around 40% apheresis due to the requirement to maintain a suitable donor base for provision of HLA-matched platelets.
- Plan to introduce pooled platelets in PAS by end of current f/y.
- Move to 60% platelet apheresis by end f/y 2015/16.
- Move to 40% apheresis by end f/y 2016/17.

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