Fibrinogen concentrate versus placebo for treatment of postpartum haemorrhage:

A multicentre, prospective, double-blind, randomised control study (OBS2)

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OBS2 Obstetric Bleeding Study 2
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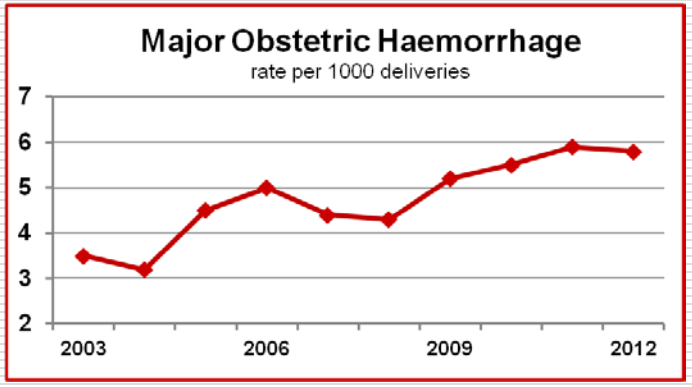
NHS Wales GIG Cymru

Background

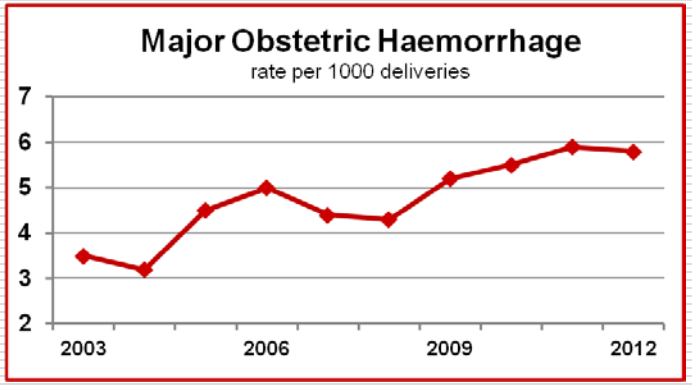
- Postpartum haemorrhage (PPH) is a significant cause of maternal morbidity[1]
- Major Obstetric Haemorrhage has an incidence of around 6 per 1000 births[1]



[1] Lennox C, Marr L. Scottish confidential audit of severe maternal morbidity. *Tenth Annual Report*. 2013

Background

- Postpartum haemorrhage (PPH) is a significant cause of maternal morbidity[1]
- Major Obstetric Haemorrhage has an incidence of around 6 per 1000 births[1]
- Low Levels of Fibrinogen (<3g/L) measured early in a PPH are associated with increased severity[2]



- FIBTEM as a Point of Care test is equally predictive of severity[2]

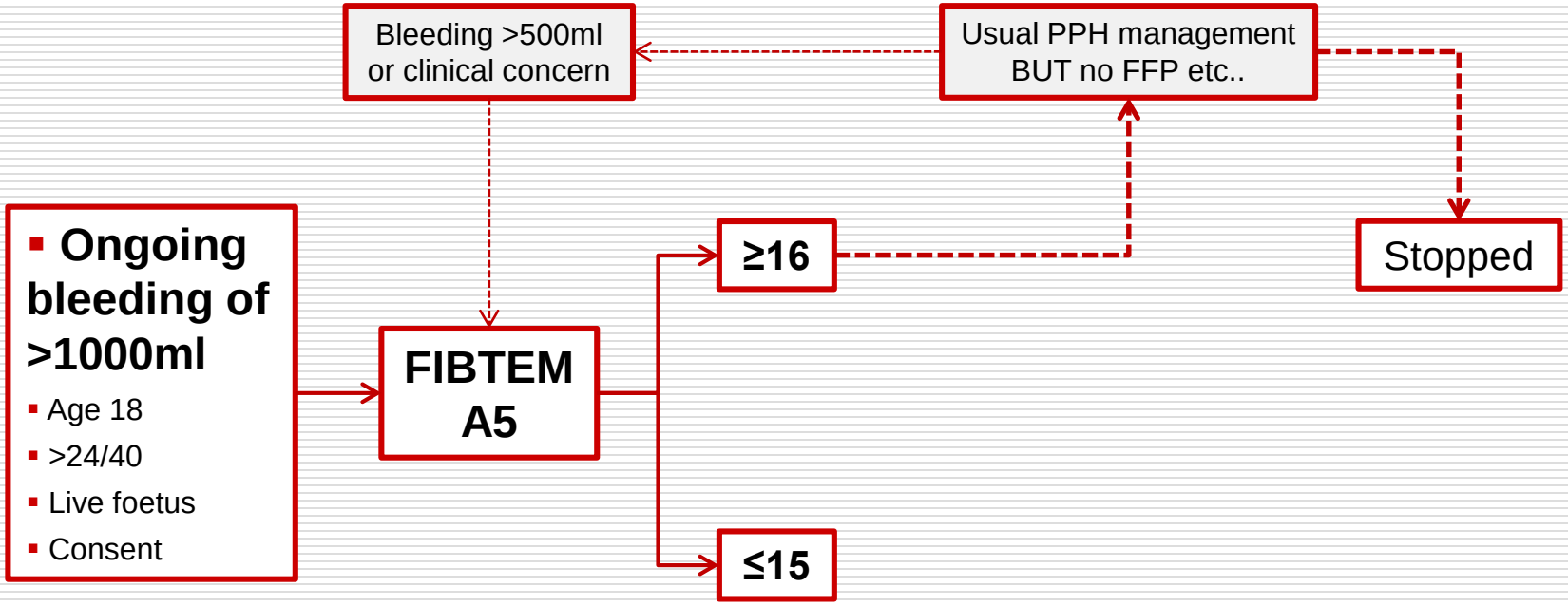
[1] Lennox C, Marr L. Scottish confidential audit of severe maternal morbidity. *Tenth Annual Report*. 2013

[2] Collins PW, et al. Fibrin-based clot formation as an early and rapid biomarker for progression of postpartum hemorrhage: a prospective study. Blood. 2014 Sep 11;124(11):1727-36

OBS2 Hypothesis

- Early administration of Fibrinogen concentrate
- Guided by a FIBTEM assay
- During a moderate to severe PPH
- Reduces allogeneic blood product usage
  - Red Blood Cells (RBC), FFP, Cryoprecipitate and Platelets

Study Design



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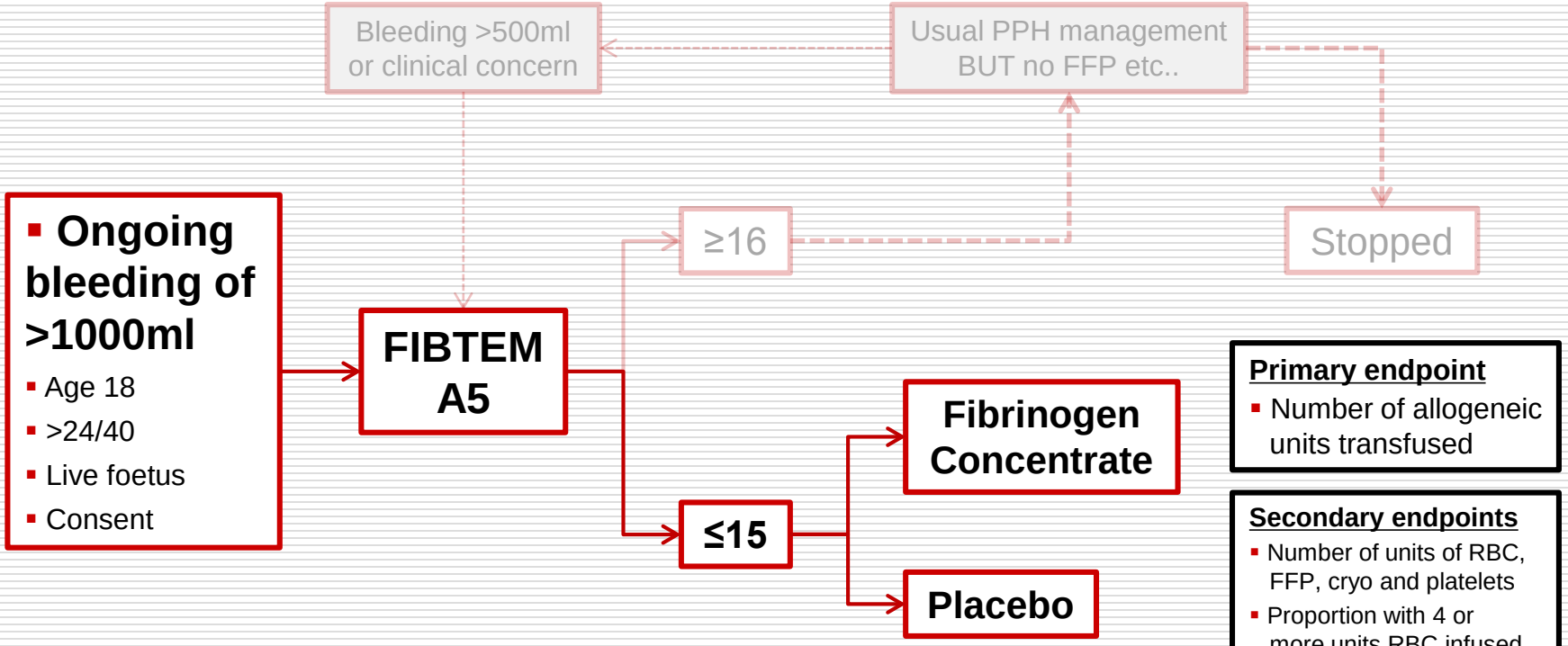


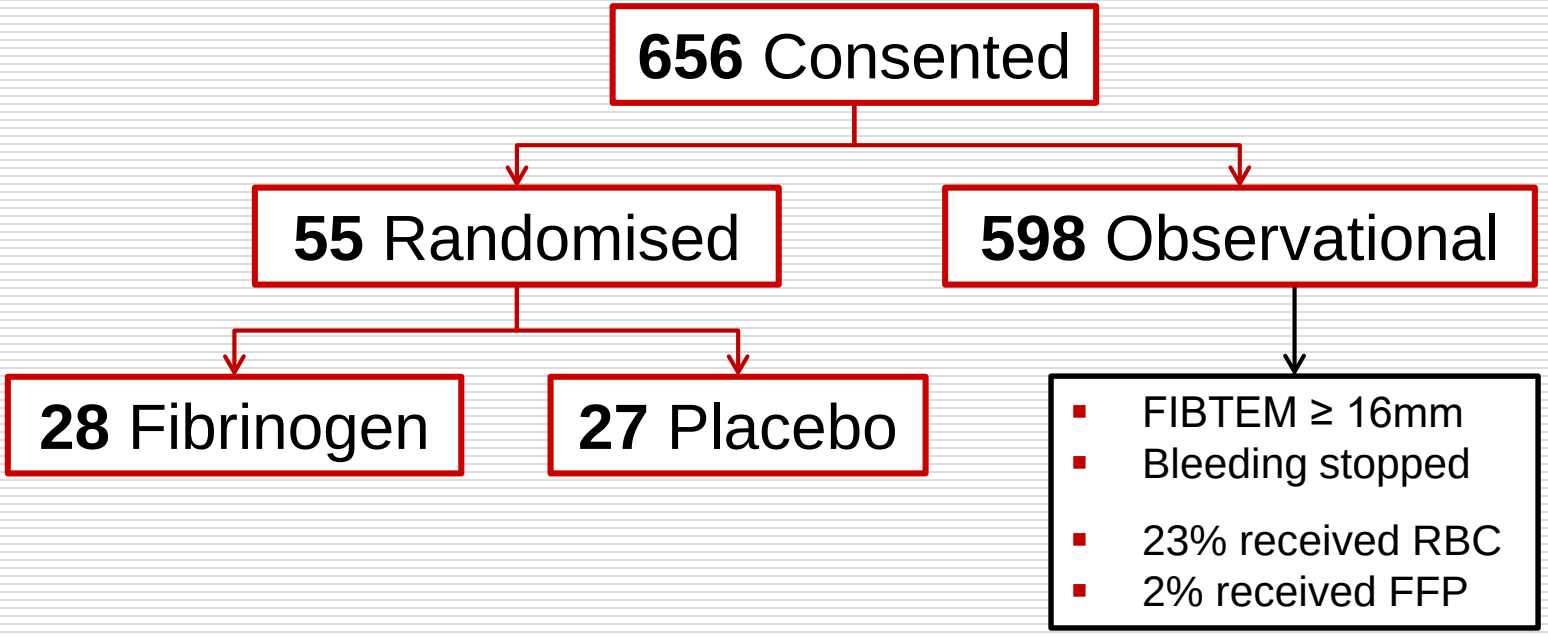
Primary endpoint

- Number of allogeneic units transfused

Secondary endpoints

- Number of units of RBC, FFP, cryo and platelets
- Proportion with 4 or more units RBC infused
- Total blood loss
- Bleeds > 2500 mL
- Invasive interventions
- ITU/HDU admission
- Economic evaluation

Results


656 Consented
55 Randomised
598 Observational
28 Fibrinogen
27 Placebo
FIBTEM ≥ 16mm
Bleeding stopped
23% received RBC
2% received FFP

Results: **Primary outcome**

	Fibrinogen (n = 28)	**Placebo** (n = 27)
Total Number of Allogeneic units	**58**	**75**
Mean (SD)	**2.07 (3.33)**	**2.78 (4.77)**

Adjusted incidence rate ratio (95% CI): 0.72 (0.30 – 1.70)

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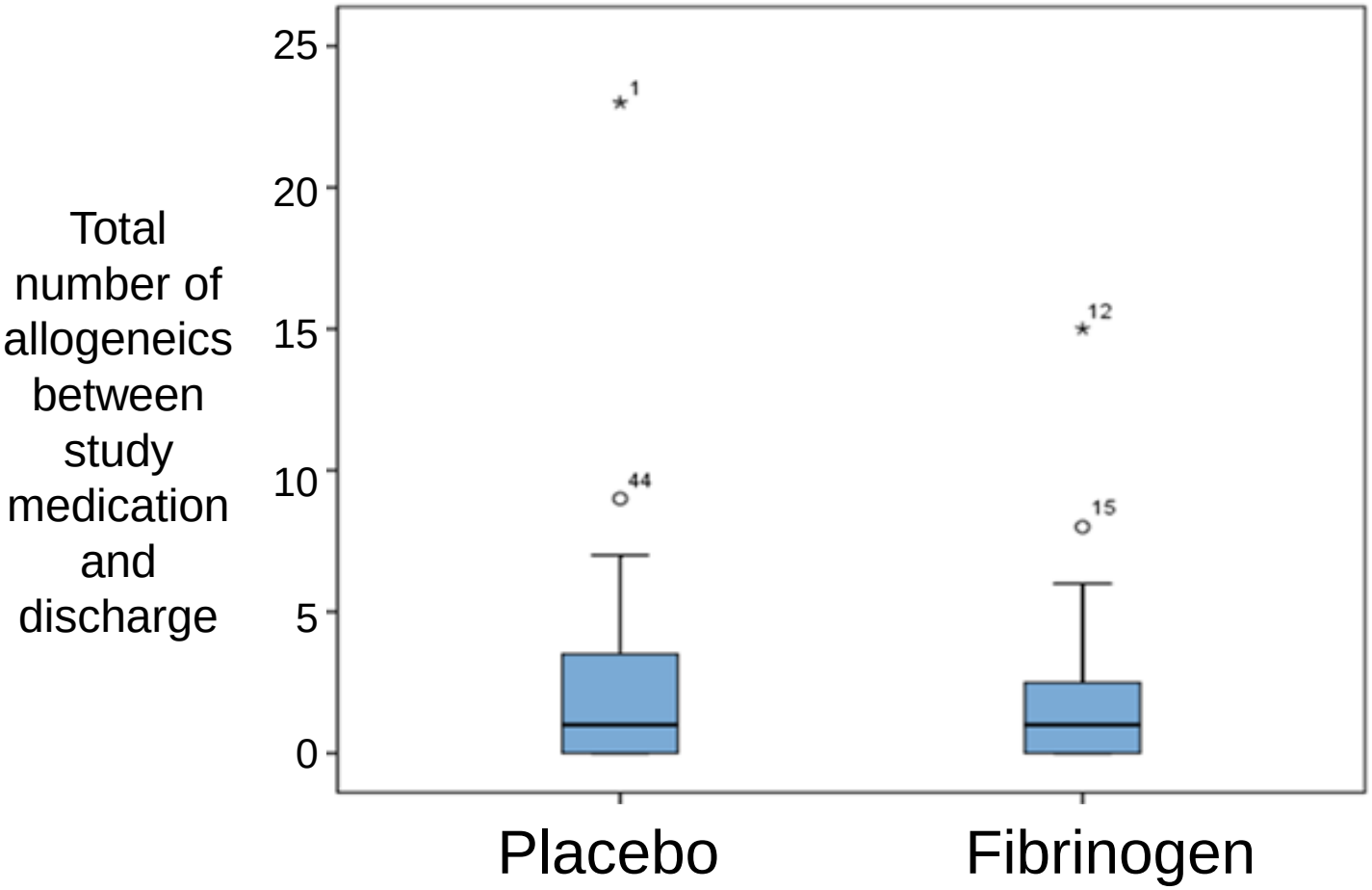
FFP transfused	18	33

Total number of allogeneic units



Results: **Pre-specified subgroup analysis**

Fibrinogen ≥ 2.0g/L :

	Fibrinogen (n = 21)	**Placebo** (n = 18)
Total Number of Allogeneic units	**18**	**21**
Median (IQR)	**0** (0-2)	**0** (0-1.8)

Results: **Pre-specified subgroup analysis**

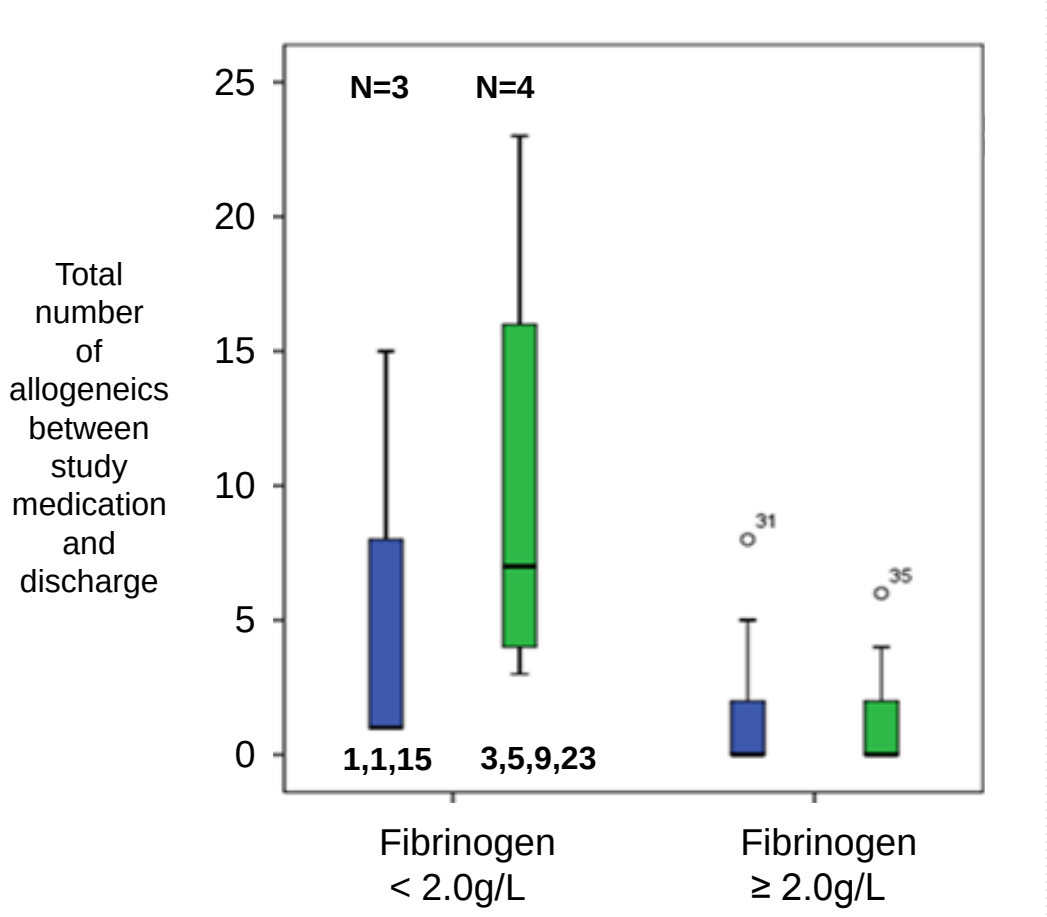
Fibrinogen ≥ 2.0g/L :

	Fibrinogen (n = 21)	Placebo (n = 18)
Total Number of Allogeneic units	18	21
Median (IQR)	**0** (0-2)	**0** (0-1.8)

Fibrinogen < 2.0g/L :

	Fibrinogen (n = 3)	**Placebo** (n = 4)
Total Number of Allogeneic units	**17**	**40**
Median (IQR)	**1** (1-8)	**7** (4-16)

Subgroup analysis: **Total number of allogeneic units**

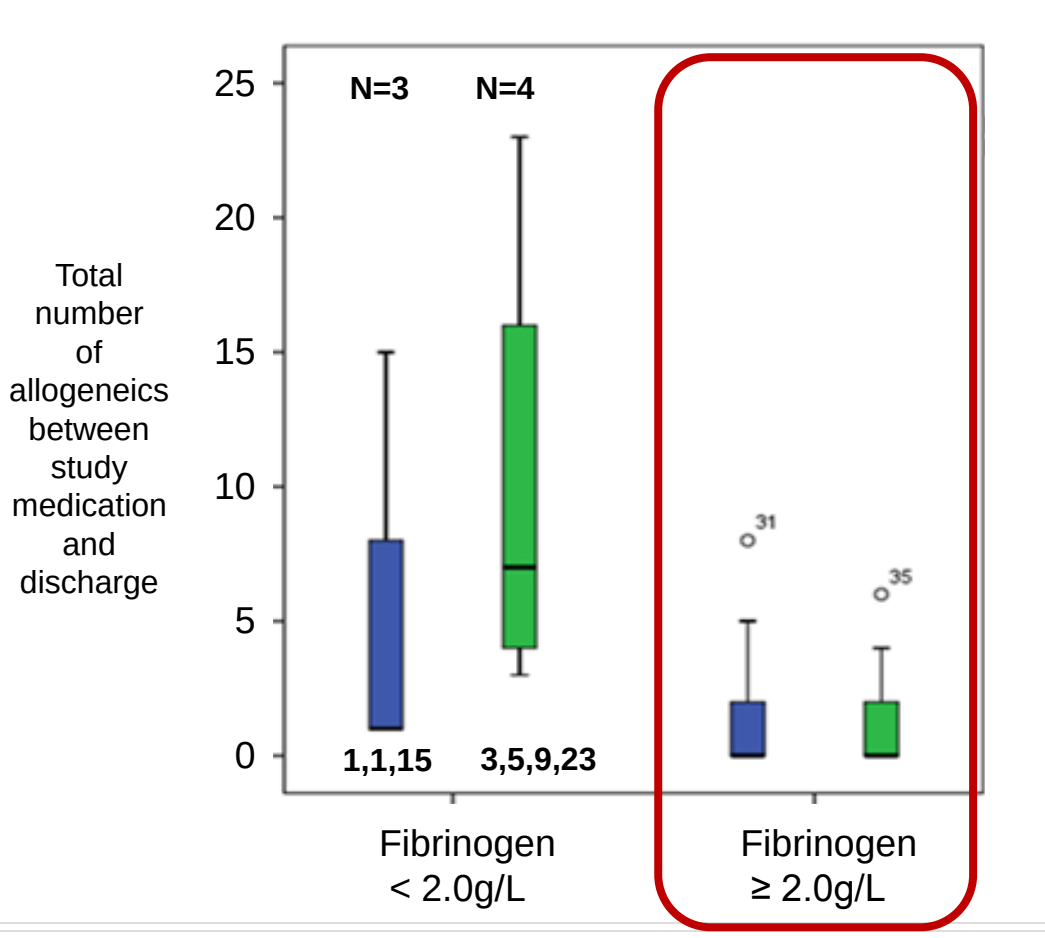


Fibrinogen

Placebo

- **Fibrinogen >2g/L:** there was no difference in blood product use
- **Fibrinogen <2g/L:** there may be a difference but numbers too small to draw conclusions

Subgroup analysis: **Total number of allogeneic units**



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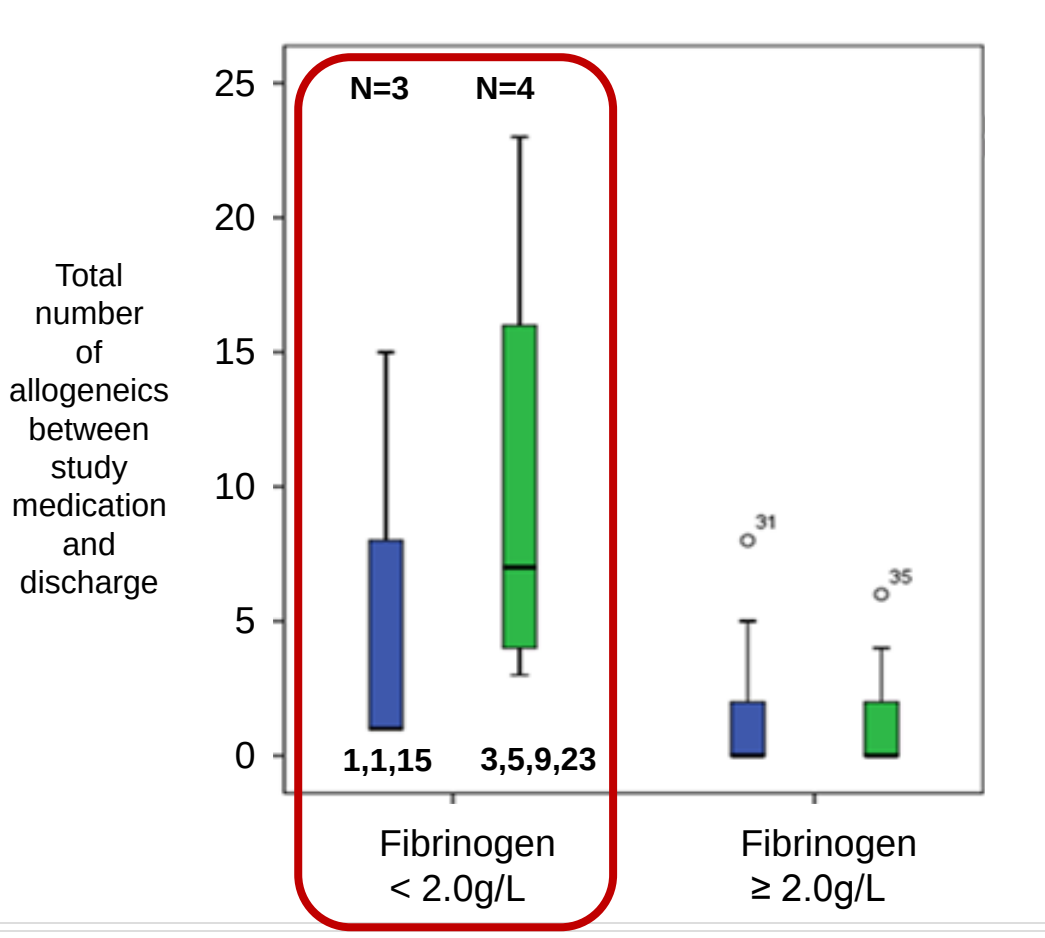

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Conclusion / Discussion

- In OBS2 haemostatic impairment was a rare event
  - Only 7/656 (1%) women had fibrinogen levels below 2.0 g/L
- Using a trigger for fibrinogen replacement of a FIBTEM A5 ≤15mm (≈ 3g/L) does not reduce allogeneic blood product usage
- No evidence that haemostatic support between fibrinogen 2-3g/L is beneficial
- Fibrinogen concentrate may be beneficial below 2g/L
- No support for unmonitored fibrinogen replacement

Acknowledgements

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