

Obstetric Haemorrhage
and
use of Viscoelastic
Assay
Thromboelastography

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Disclosures

NHS consultant

Cardiff University honorary lecturer

PI Obstetric Bleeding Study 'plus'

Study support from
Haemanetics, OAA, NIAA



Lecture objectives

PPH- adaptations in pregnancy

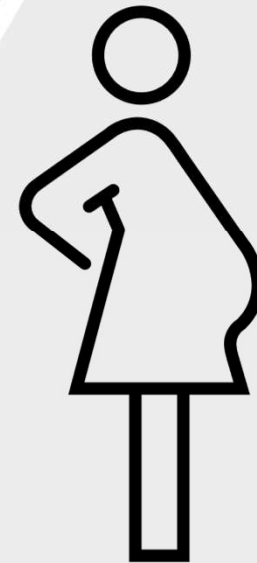
PPH- impact and recognition

Coagulopathy in PPH

Role of Visco haemostatic assays
(VHA) in PPH

Coagulation in pregnant women at term

- Fibrinogen 4-6 g/L
- Blood volume 100 ml/Kg
- Increased pro-coagulant
- Reduced anticoagulant

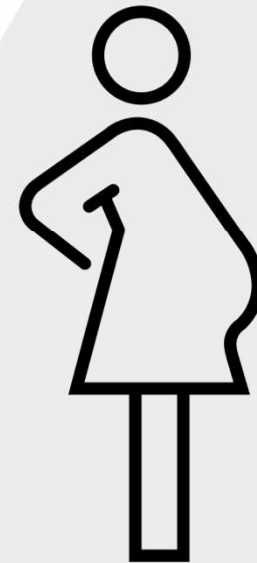


Coagulation in pregnant women at term

- Fibrinogen 4-6 g/L
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- Increased pro-coagulant
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Non-pregnancy

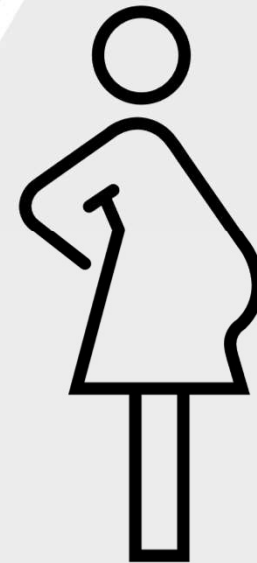
- Fibrinogen 2-4 g/L
- Blood volume 70 ml/Kg



Incidence of Coagulopathy in PPH

Coagulopathy in PPH Rare

- Low Fibrinogen $<2\text{g/L}$
5% moderate PPH
- APTT/ PT $>1.5\text{x}$ normal range
 $<1\%$ moderate PPH



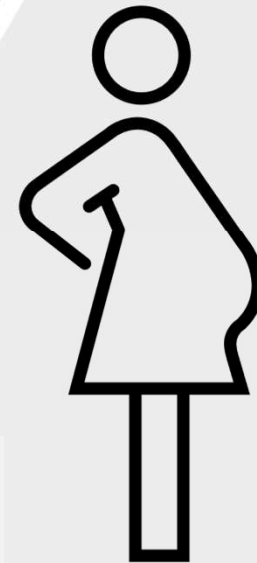
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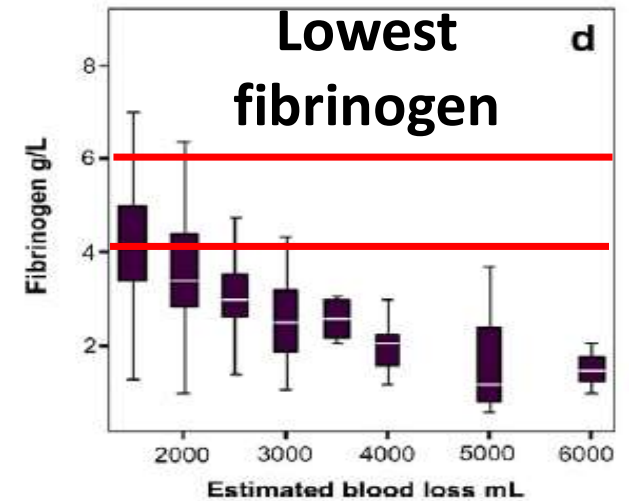
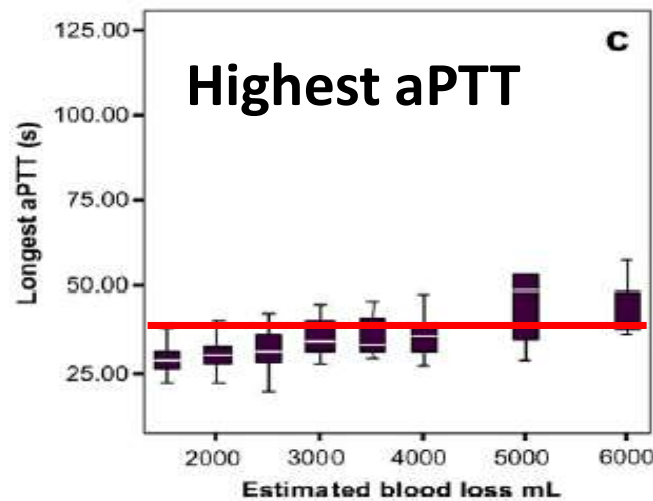
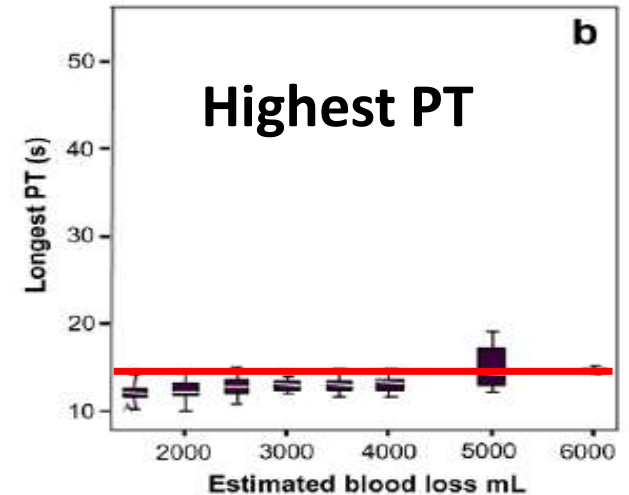
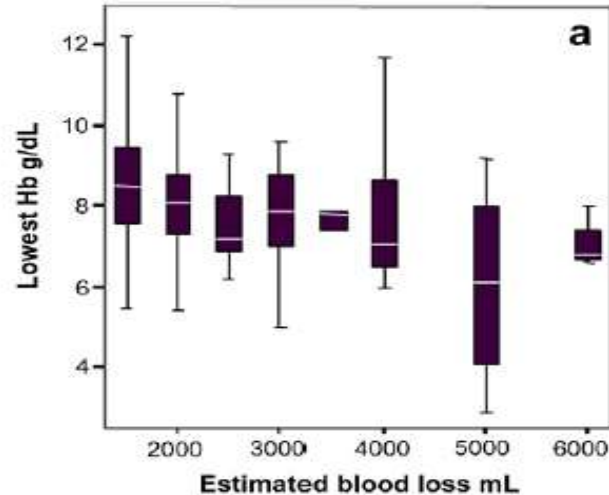
Trauma Induced Coagulopathy (TIC) in severely injured non-pregnant adults

- Common, 30%



What does coagulopathy in PPH look like?

- PT and APTT remain normal until very large bleed volumes
- Fibrinogen falls early and reaches critical levels earliest in PPH





Study cohort: Aim to describe the coagulopathy of PPH

- Recruitment
 - Bleed ≥ 1000 mL or clinical concern (Abruption/AFE)
- Enrolled
 - Postpartum haemorrhage N=518/10790 (4.8%)
 - Non-bleeding pregnant (before elective c section) N=38
- Total blood loss
 - Median (IQR) range 1500 (1205-1800) 200-8500
- Transfusion
 - Red cells: N=133
 - Fibrinogen: N=19
 - Platelets: N=7
 - FFP: N=3
- Inclusion rate
 - ≥ 1000 n=495 (50%) of available bleeds
 - ≥ 1500 n=274 (78%) of available bleeds
 - ≥ 2500 n=39 (100%) of available bleeds

Amniotic Fluid Embolus- severe obstetric coagulopathy

Classical catastrophic maternal
collapse

Distinct, severe coagulopathy

Massive fibrinolysis

- Fibrin degradation (D-dimers)
- Massive plasmin activation (PAP)
- Low functional Fibrinogen



Massive hyperfibrinolysis in PPH

Massive hyperfibrinolysis found in 0.2% recruits in OBSplus study

‘Acute Obstetric coagulopathy’

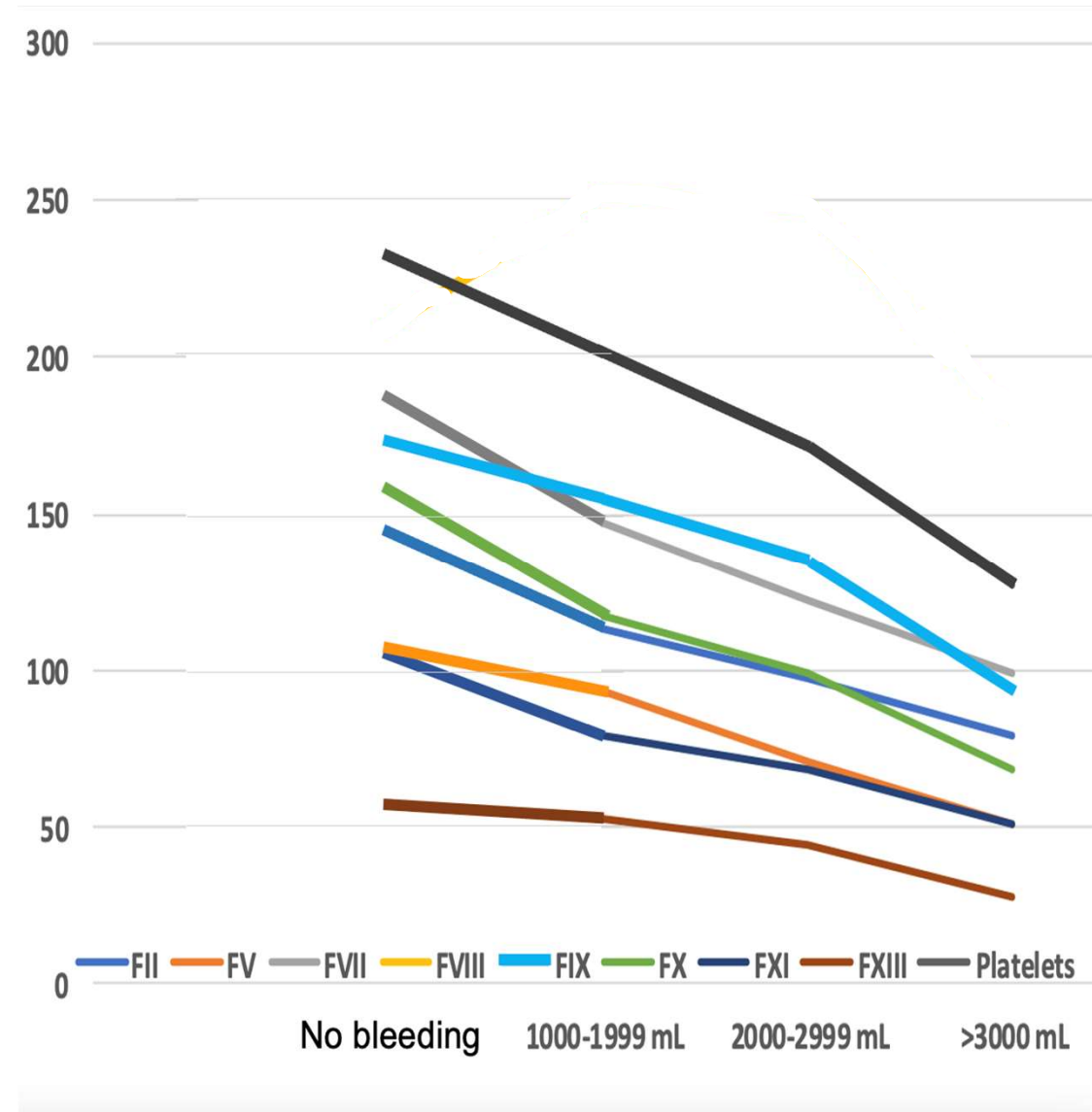
- Diverse presentation and aetiologies
- 50% associated with intra-uterine or neonatal death
- Rare
2% cases, 1/1000 deliveries



Coagulation factor levels by bleed volume in PPH without massive Fibrinolysis

Women with severe PPH

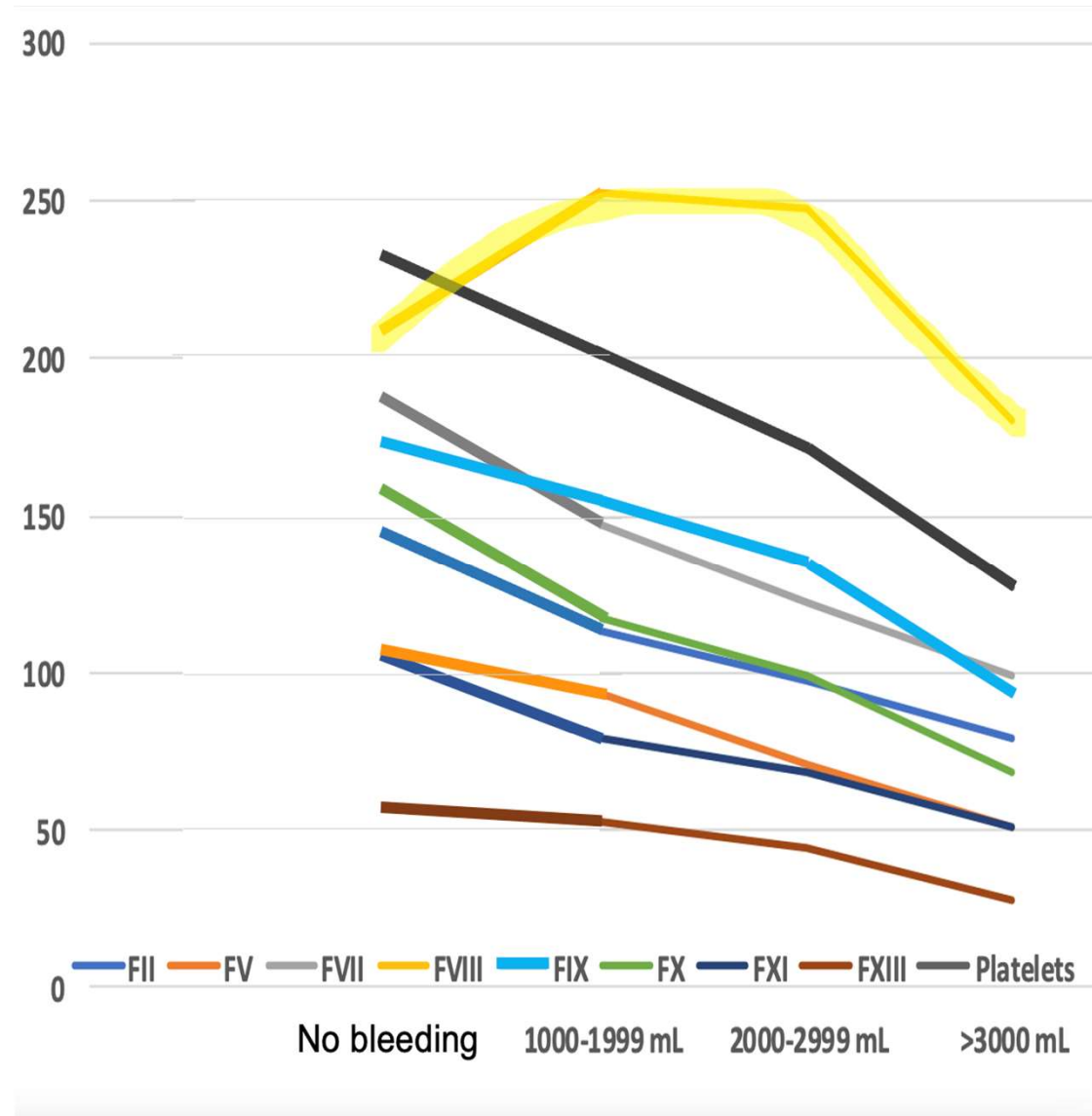
- Linear decrease in clotting factors and plt with increasing bleed volume
- Dilution of clotting factors blood loss and fluid resuscitation



Coagulation factor levels by bleed volume in PPH without massive Fibrinolysis

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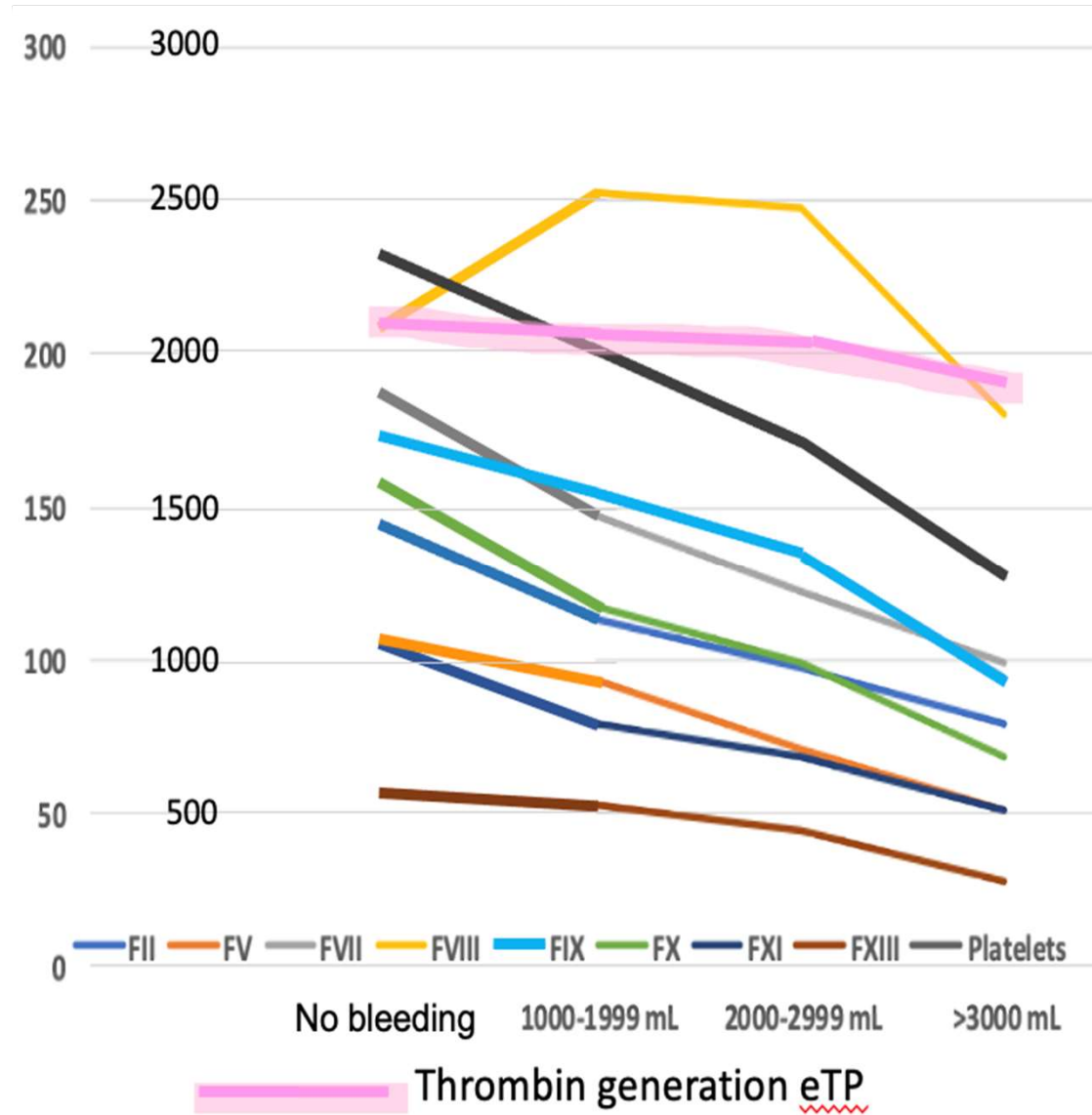
- Linear decrease in clotting factors and plt with increasing bleed volume
- Dilution of clotting factors blood loss and fluid resuscitation
- Factor FVIII (procoagulant) increased



Coagulation factor levels by bleed volume in PPH without massive Fibrinolysis

Thrombin generation mTP maintained

- Overall clotting factor function preserved up to 3L blood loss



Targets for coagulation in PPH

Fibrinogen $>2\text{g/L}$ = primary target

Early TXA improves outcomes (WOMAN Trial)

Keep APTT/PT $<1.5\times$ normal

- FFP – non pregnant donors, Fibrinogen content approx. 2 g/L
- Unsuitable for rapid correction fibrinogen $<2\text{g/L}$
- Risk of fluid overload, TRALI with large volumes of FFP
- Unnecessary transfusion in most women
- Cryo or Fibrinogen concentrate- high concentrations of Fibrinogen

Laboratory tests of coagulation

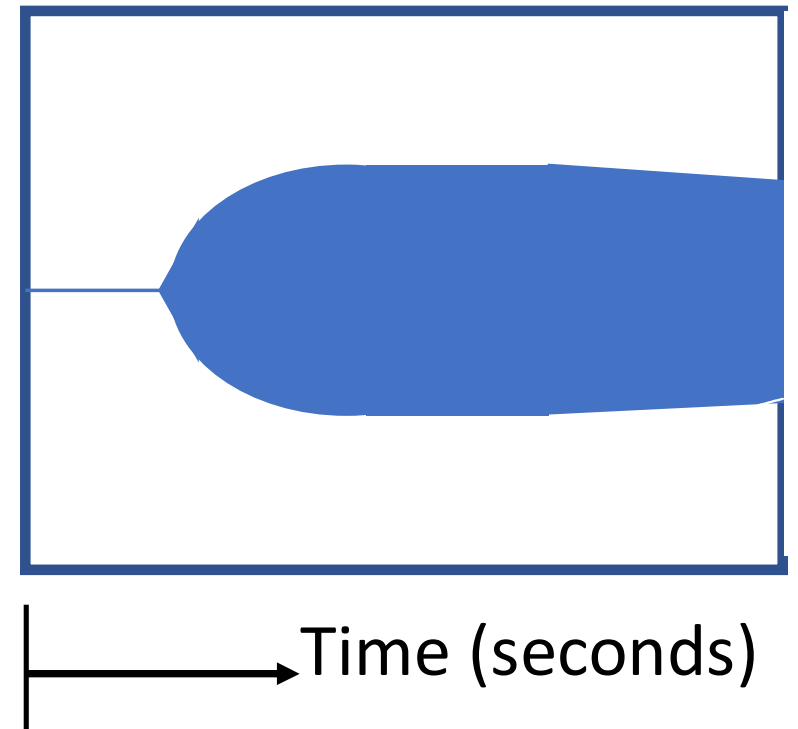
- 45 – 60 minutes turnaround
 - Too slow to inform clinical decisions
- = Empirical treatment decisions



Viscoelastic Thromboelastography Tests (ROTEM, TEG)

- **Visual report of clot formation**
- Whole blood
- Rapid results - 10 minutes

= Guide coagulation treatment decisions





MBRRACE-UK

Mothers and Babies: Reducing Risk through
Audits and Confidential Enquiries across the UK

Haemorrhage
and AFE

December 2020

Many women who died had delayed or
inadequate correction of their coagulopathy

VHA devices can minimise delays but must be
interpreted correctly

How to resuscitate in PPH?

- Greentop RCO&G- Expert consensus for empiric treatment

**FFP 12-15ml/Kg after 4 units RBC have been transfused
(0.6g fibrinogen /unit, 900ml= 1.8g Fibrinogen)**

Earlier if coagulopathy anticipated- Abruption, AFE, delayed recognition of bleeding

>12-15 ml/Kg may be required for APTT/ PT >1.5 x N

How to resuscitate in PPH?

Timely RBC transfusion

- POC Hb guide
- Lactate / shock status
- Clinical evaluation



VHA Tests in PPH- guidance

- **NICE 2014**

Call for more evidence in PPH

- **RCOG, Greentop 2016**

Use alongside laboratory tests, with an agreed treatment algorithm

- **BSH Guideline 2018**

Use with an agreed treatment algorithm

Do not use to withhold TXA



OBS+ Study

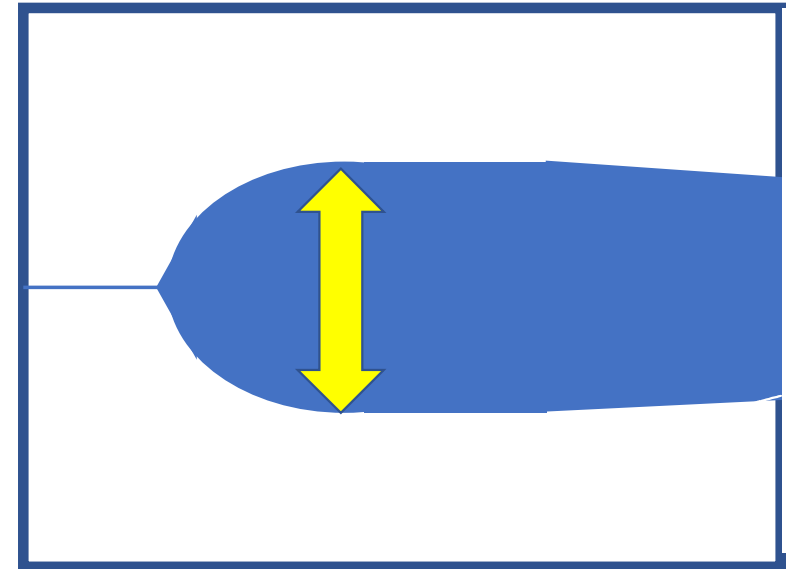
- Sensitivity and specificity of **VHA intervention thresholds in PPH**
- ROTEM Sigma 522 samples matched with laboratory assays
- TEG 6s 389 samples matched with laboratory assays

1. S.F. Bell et al. The sensitivity and specificity of rotational thromboelastometry (ROTEM) to detect coagulopathy during moderate and severe postpartum haemorrhage: a prospective observational study, IJOA 2022 February ;49: 103238

2. Roberts TCD et al. Utility of viscoelastography with TEG 6s to direct management of haemostasis during obstetric haemorrhage: a prospective observational study. IJOA 2021 Aug ;47:103192

Fibrinogen estimation by VHA

- Platelet inhibitor added to citrated blood
- Clot amplitude at 5, 10 minutes
- Measures contribution of Fibrinogen to the clot

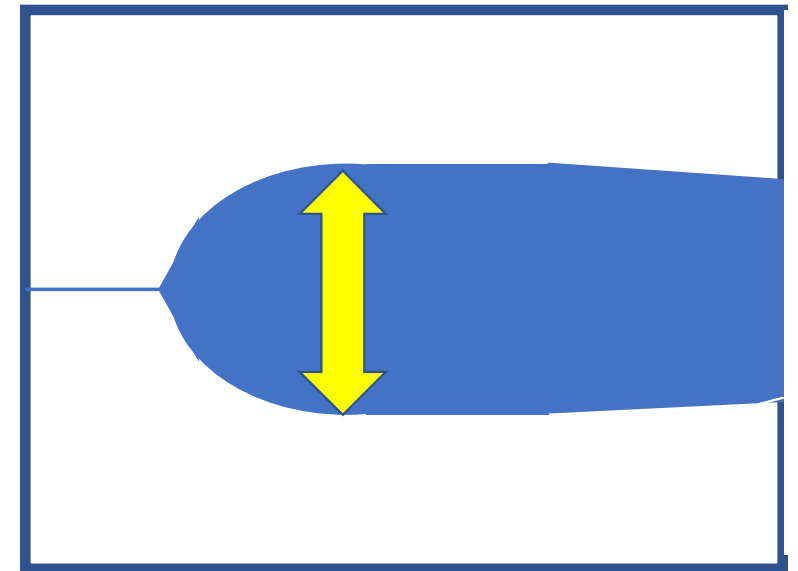


Incidence Fibrinogen <2g/L 5% in study

Fibrinogen replacement- Clauss Fibrinogen $\leq 2\text{g/L}$

- **ROTEM Fibtem A5 $\leq 11\text{mm}$**
- **<ROC 0.96 (95% CI 0.94 to 0.98)**
- **Sensitivity 0.76 specificity 0.96**
- **PPV 0.57 NPV 0.98**

- **TEG CFF $\leq 17\text{ mm}$**
- **ROC 0.95 (0.91 to 0.99), $P < 0.0001$**
- **Sensitivity 0.74 specificity 0.97**
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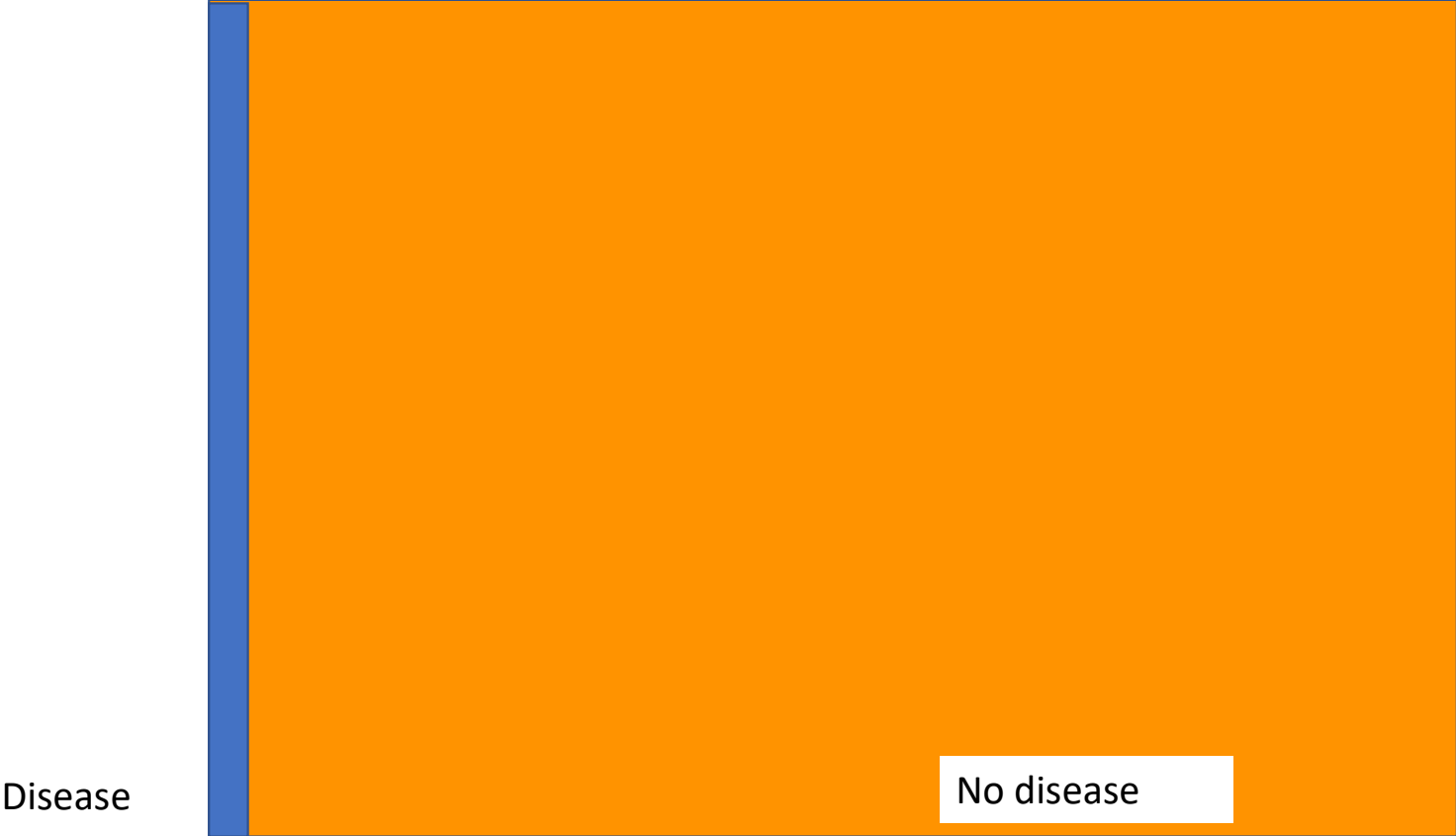
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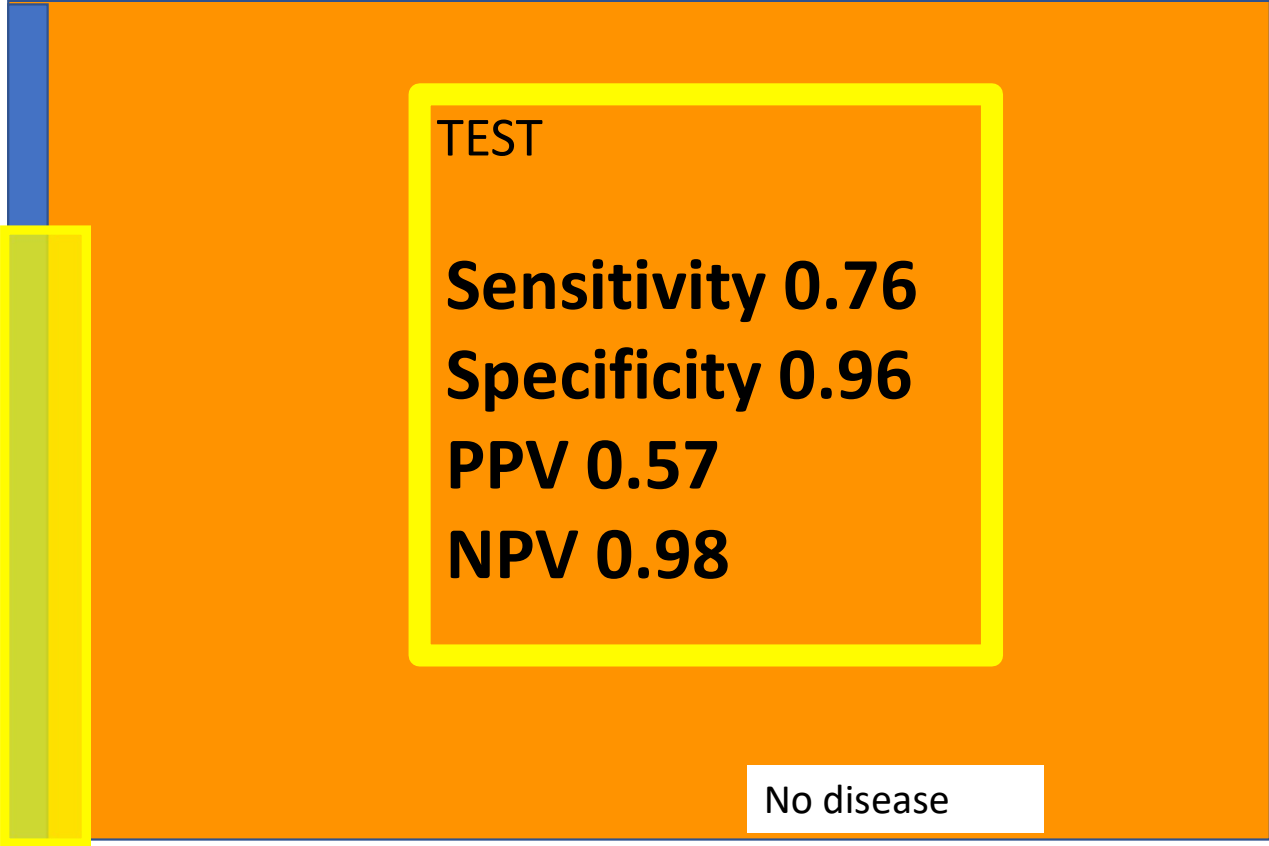
Is a test with
50%
Positive predictive value
useful ?

Population with low disease prevalence



Population with low disease prevalence

TEST



Disease

No disease

Population with low disease prevalence

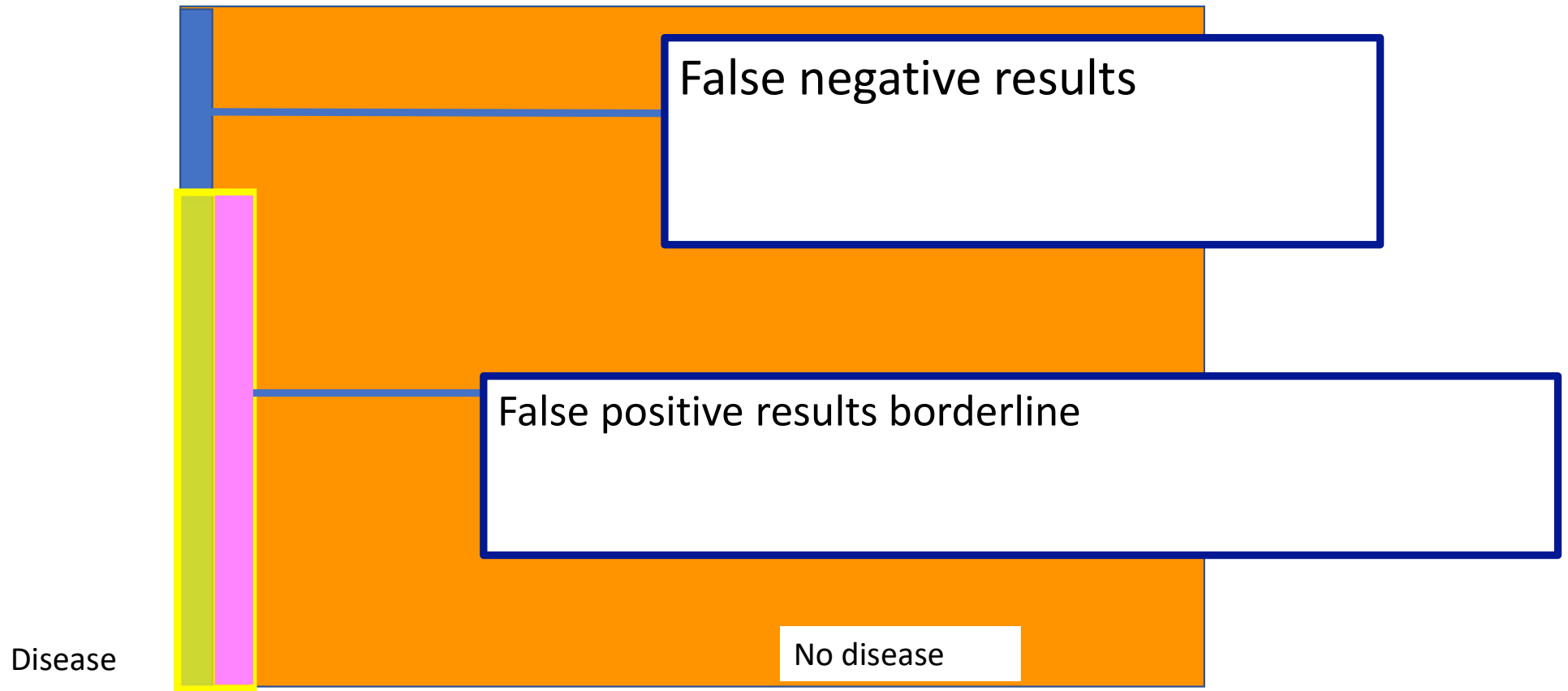
TEST

Disease

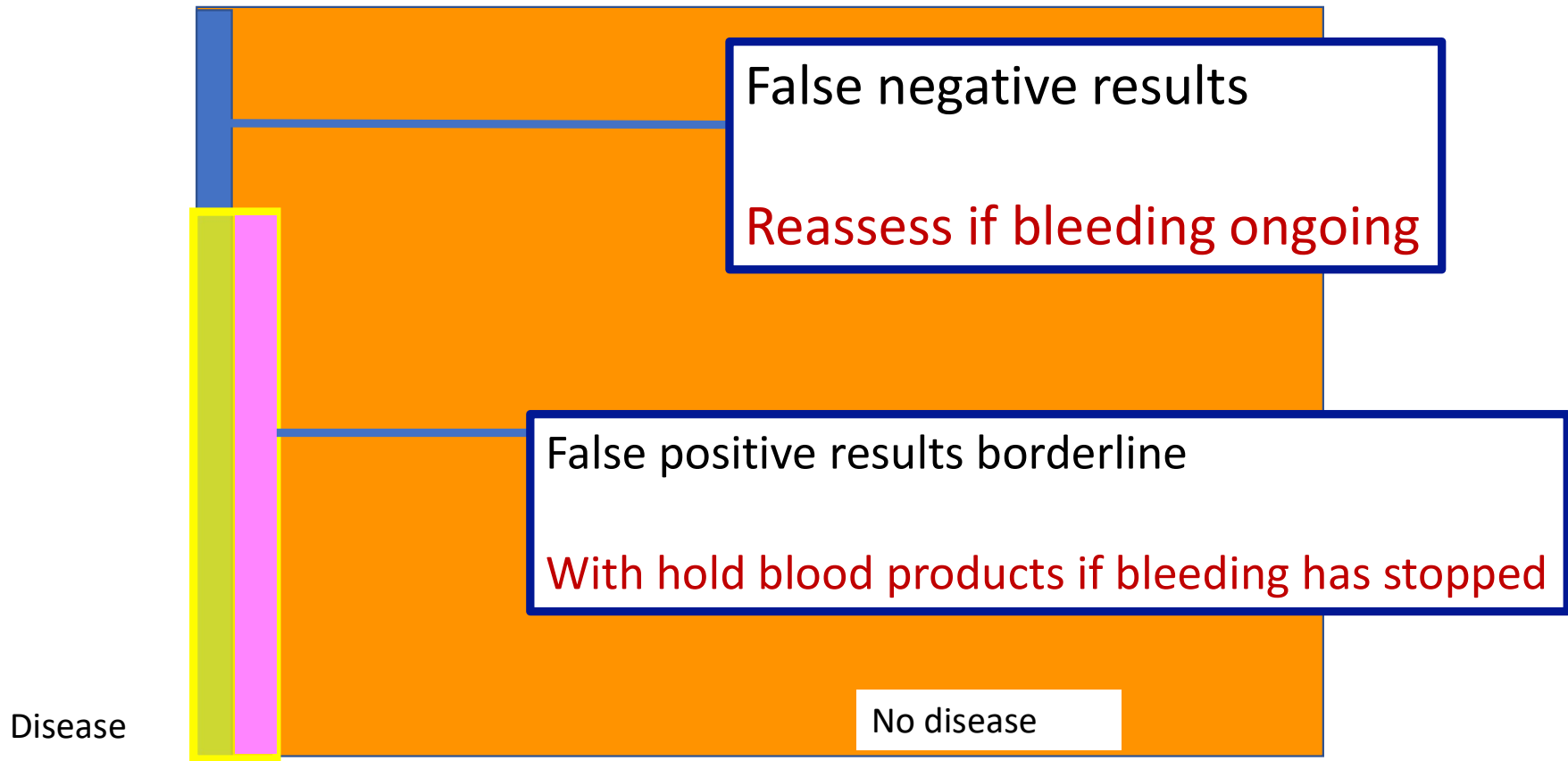


No disease

Population with low disease prevalence- Added value of clinical context & algorithm



Population with low disease prevalence- Added value of clinical context & algorithm



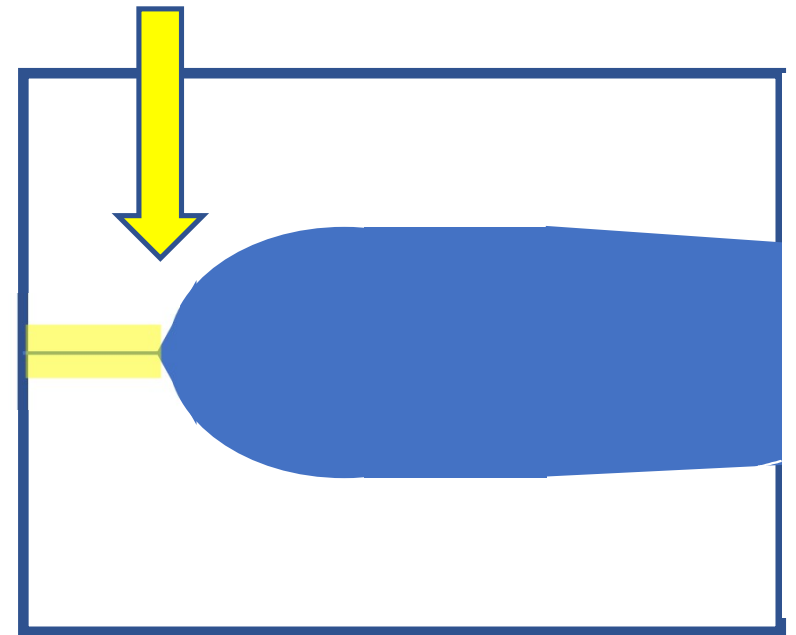
Fibrinogen replacement

Primary target in PPH >2g/L

- Evidence based Thresholds described for ROTEM and TEG6s
- **Rotem Sigma Fibtem A5 11mm¹**
- **TEG 6S CFF (by 10) 17mm²**

FFP infusion - APTT/ PT estimation by VHA

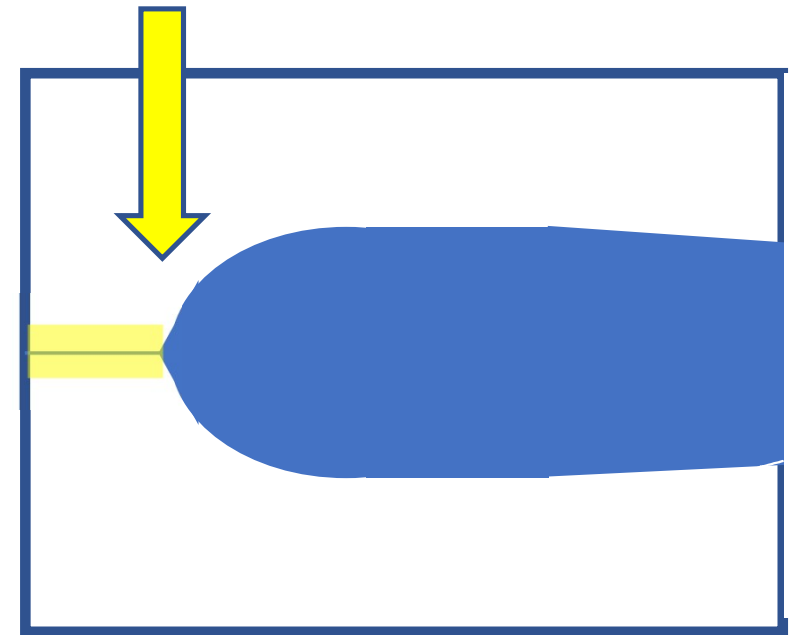
- Clot initiation time used to estimate clotting factor adequacy
- RCOG infuse FFP if APTT/PT $>1.5 \times$ normal range
- Incidence $<1\%$ in OBS+
- Detection of **any** prolonged PT/APTT



FFP infusion – Any prolonged APTT/ PT

- **EXTEM CT >75 seconds**
- ROC 0.81 (95% CI 0.73 to 0.88)
- **Sensitivity 0.22 Specificity 0.98**
- PPV 0.41 **NPV 0.95**

- **CK-R >7.6 minutes**
- ROC 0.82 (0.73 to 0.91), P<0.001
- **Sensitivity 0.2 specificity 0.99**
- PPV 0.67 **NPV 0.96**



FFP Infusion

- APTT/ PT >1.5 x normal range very rare
- Strong NPV and Specificity of test
- Normal EXTEM CT or CK-R -> reassuring to withhold FFP
- Consider in bleeds $>3L$ if bleeding is ongoing

Platelets infusion $<75 \times 10^9/L$

- 2% samples had plt $<75 \times 10^9/L$
- Platelets
(whole blood MA – Fibrinogen assay MA)

Platelets

Pltem <17mm

ROC 0.93 (0.87- 0.99)

Sensitivity 0.4 Specificity 0.99

PPV 0.36 NPV 0.99

CRT MA<57mm (CFF >15mm)

ROC 0.91 (0.82 to 0.99)

Sensitivity 0.5 Specificity 1

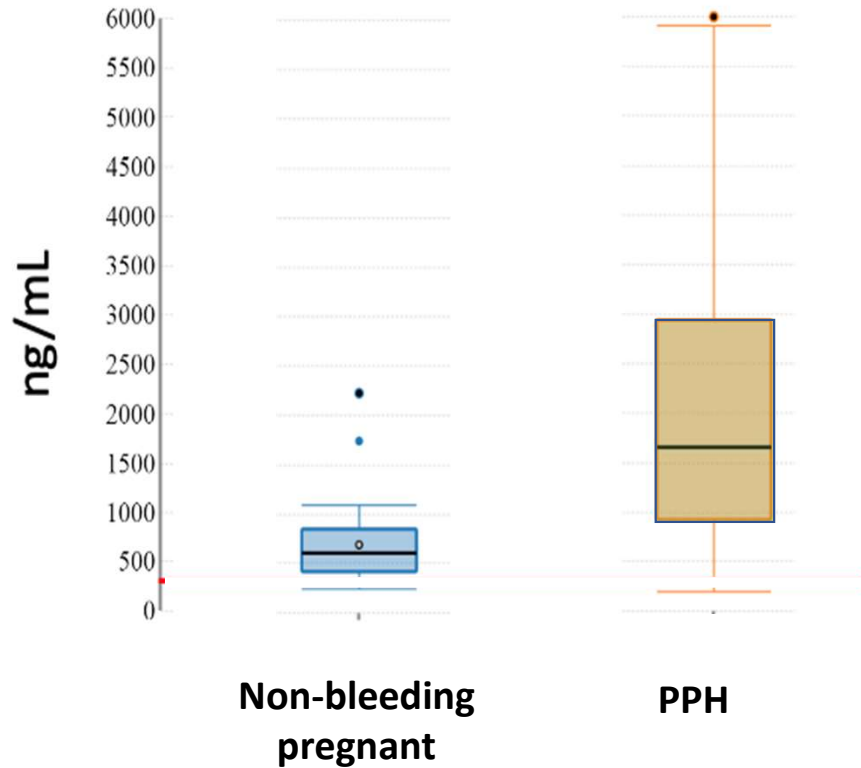
PPV 0.8 NPV 0.99

Platelets

- Strong NPV and Specificity are reassuring that platelets are not required
- Rapid turnaround FBC Gold Standard test

Fibrinolysis

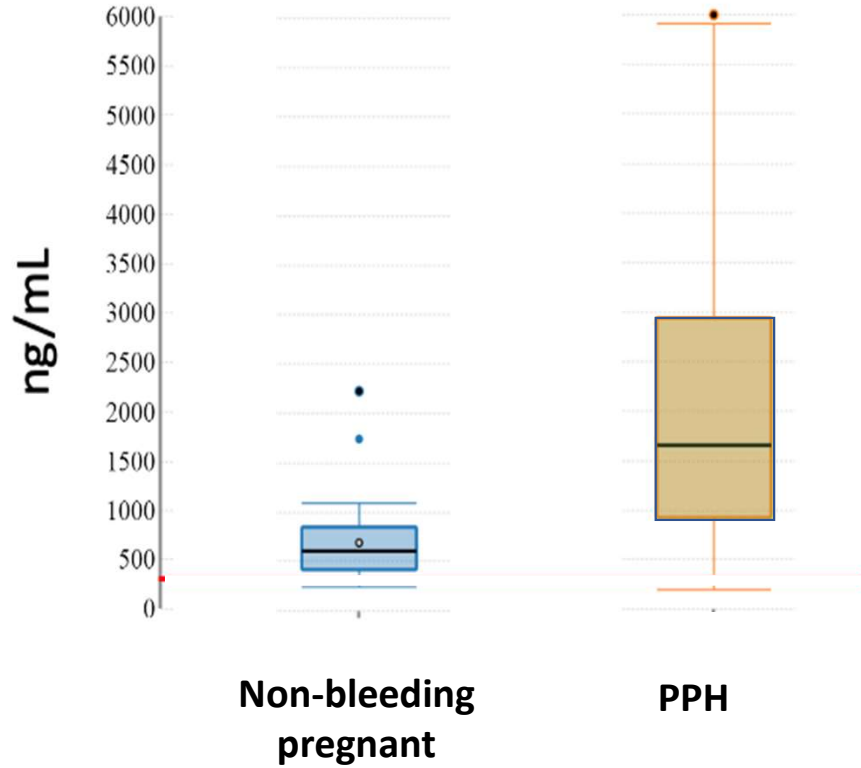
D-dimer levels in OBS+ study



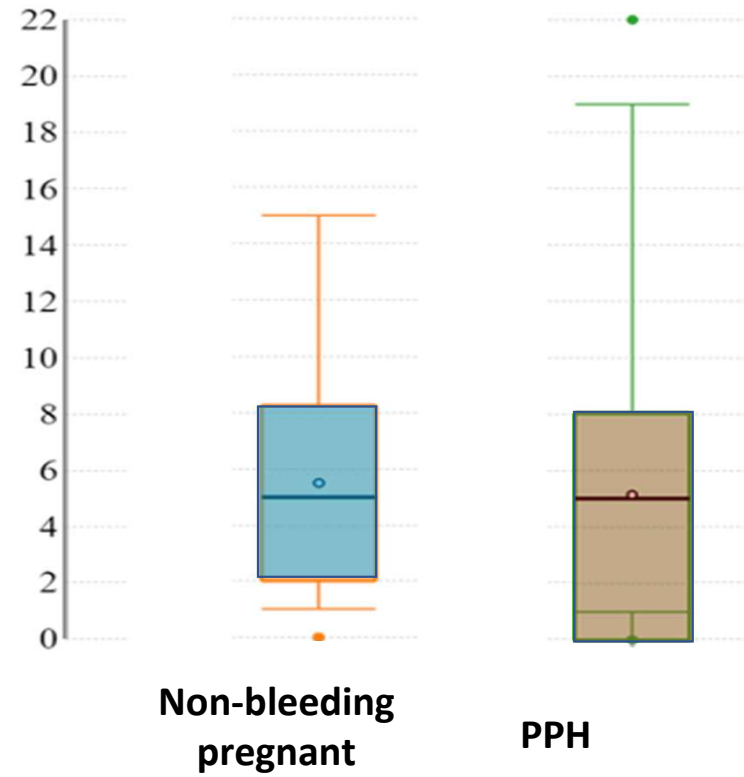
D-dimers are a laboratory marker of fibrinolysis

Fibrinolysis

D-dimer levels in OBS+ study



VHA Maximum clot lysis in OBS+ study



Fibrinolysis

Tranexamic acid routinely advised in severe PPH

Give at 1000ml if bleeding ongoing

Should not be guided by VHA

How to apply results

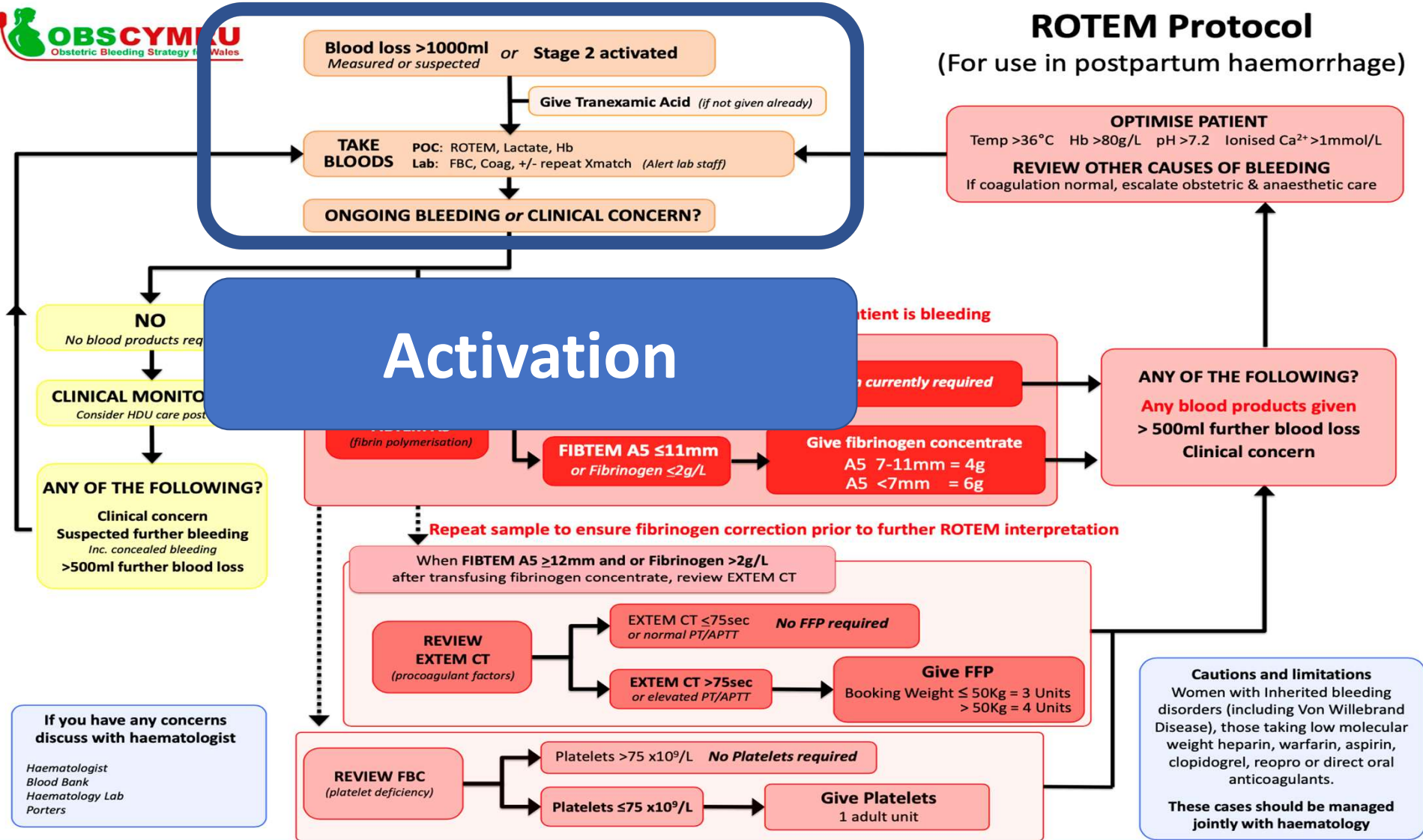
- Locally agreed algorithm

BJH OAA MBRRACE



ROTEM Protocol

(For use in postpartum haemorrhage)



If you have any concerns discuss with haematologist

Haematologist
Blood Bank
Haematology Lab
Porters

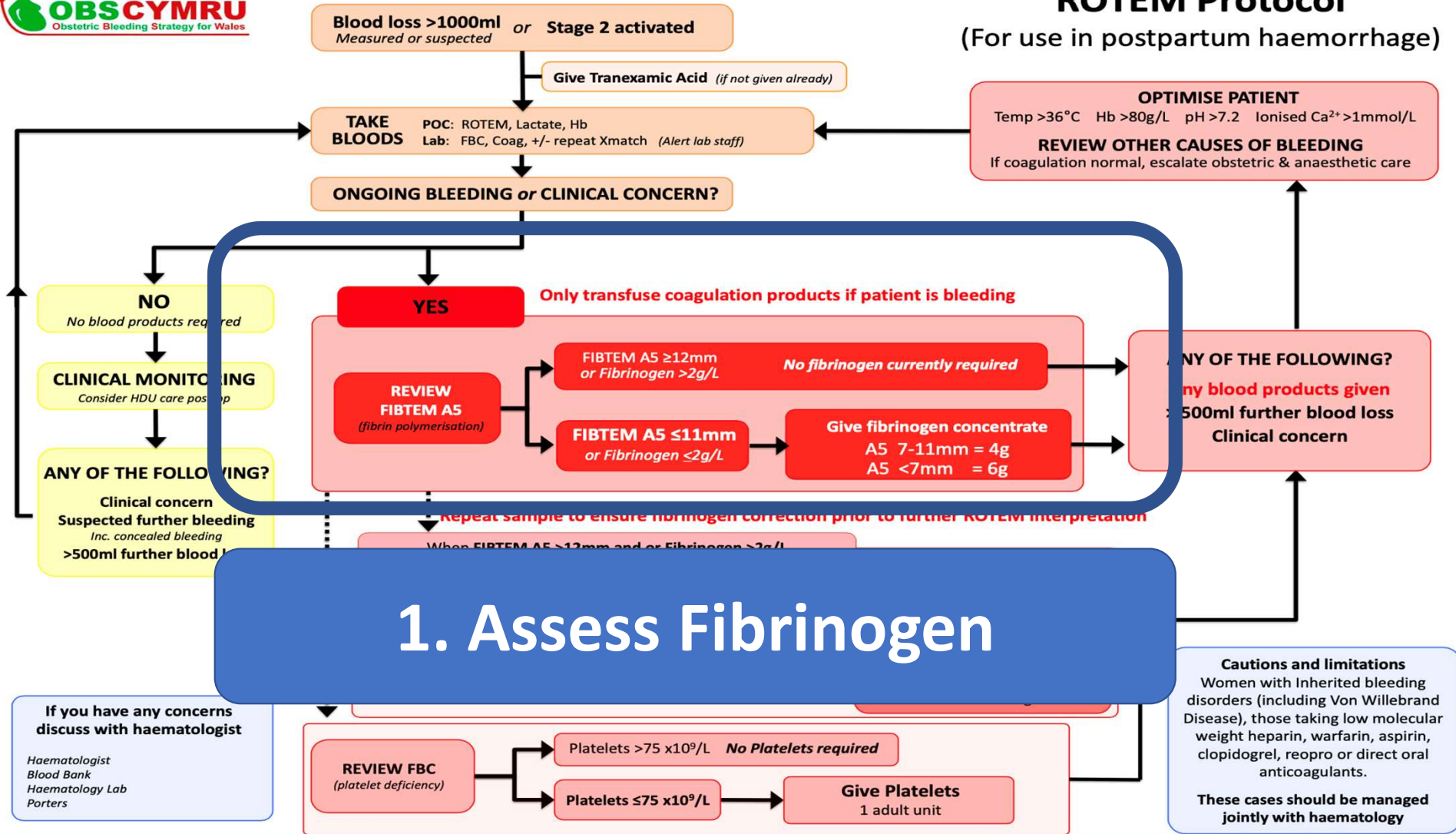
Cautions and limitations

Women with Inherited bleeding disorders (including Von Willebrand Disease), those taking low molecular weight heparin, warfarin, aspirin, clopidogrel, reopro or direct oral anticoagulants.

These cases should be managed jointly with haematology

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(For use in postpartum haemorrhage)



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ROTEM Protocol

(For use in postpartum haemorrhage)

Blood loss >1000ml or **Stage 2 activated**
Measured or suspected

Give Tranexamic Acid (if not given already)

TAKE BLOODS POC: ROTEM, Lactate, Hb
 Lab: FBC, Coag, +/- repeat Xmatch (Alert lab staff)

OPTIMISE PATIENT
 Temp >36°C Hb >80g/L pH >7.2 Ionised Ca²⁺ >1mmol/L
REVIEW OTHER CAUSES OF BLEEDING
 If coagulation normal, escalate obstetric & anaesthetic care

ONGOING BLEEDING or **CLINICAL CONCERN?**

2. Assess for FFP after Fibrinogen correction

NO
 No blood products required

CLINICAL MONITOR
 Consider HDU care post-op

ANY OF THE FOLLOWING:
 Clinical concern
 Suspected further bleeding
 Inc. concealed bleeding
 >500ml further blood loss

ANY OF THE FOLLOWING?
 No blood products given
 Further blood loss
 Clinical concern

Repeat sample to ensure fibrinogen correction prior to further ROTEM interpretation

When **FIBTEM A5 ≥12mm** and or **Fibrinogen >2g/L** after transfusing fibrinogen concentrate, review EXTEM CT

REVIEW EXTEM CT (procoagulant factors)
 EXTEM CT ≤75sec or normal PT/APTT **No FFP required**

EXTEM CT >75sec or elevated PT/APTT
Give FFP
 Booking Weight ≤ 50Kg = 3 Units
 > 50Kg = 4 Units

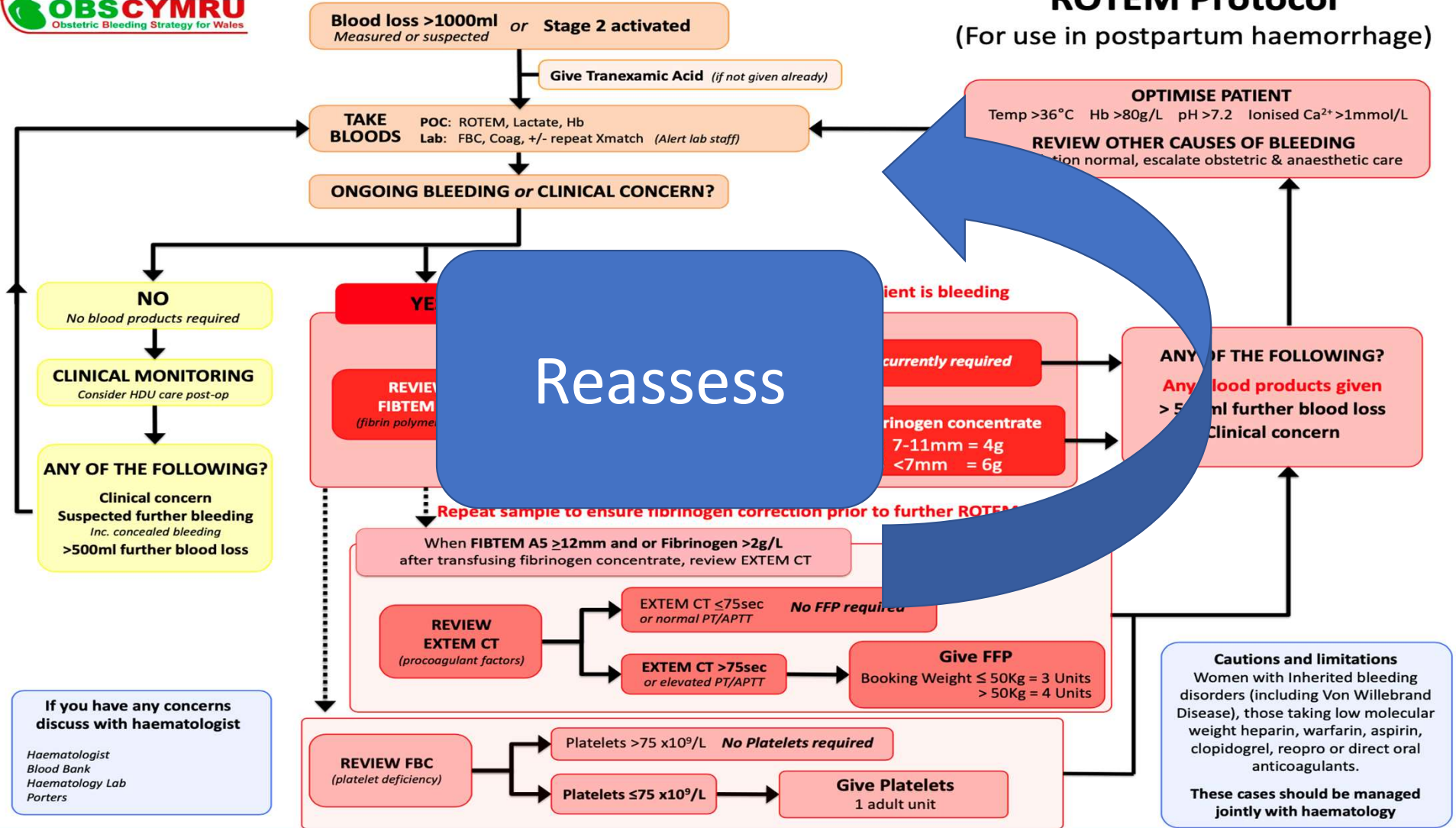
REVIEW FBC (platelet deficiency)
 Platelets ≤75 x10⁹/L
Give Platelets
 1 adult unit

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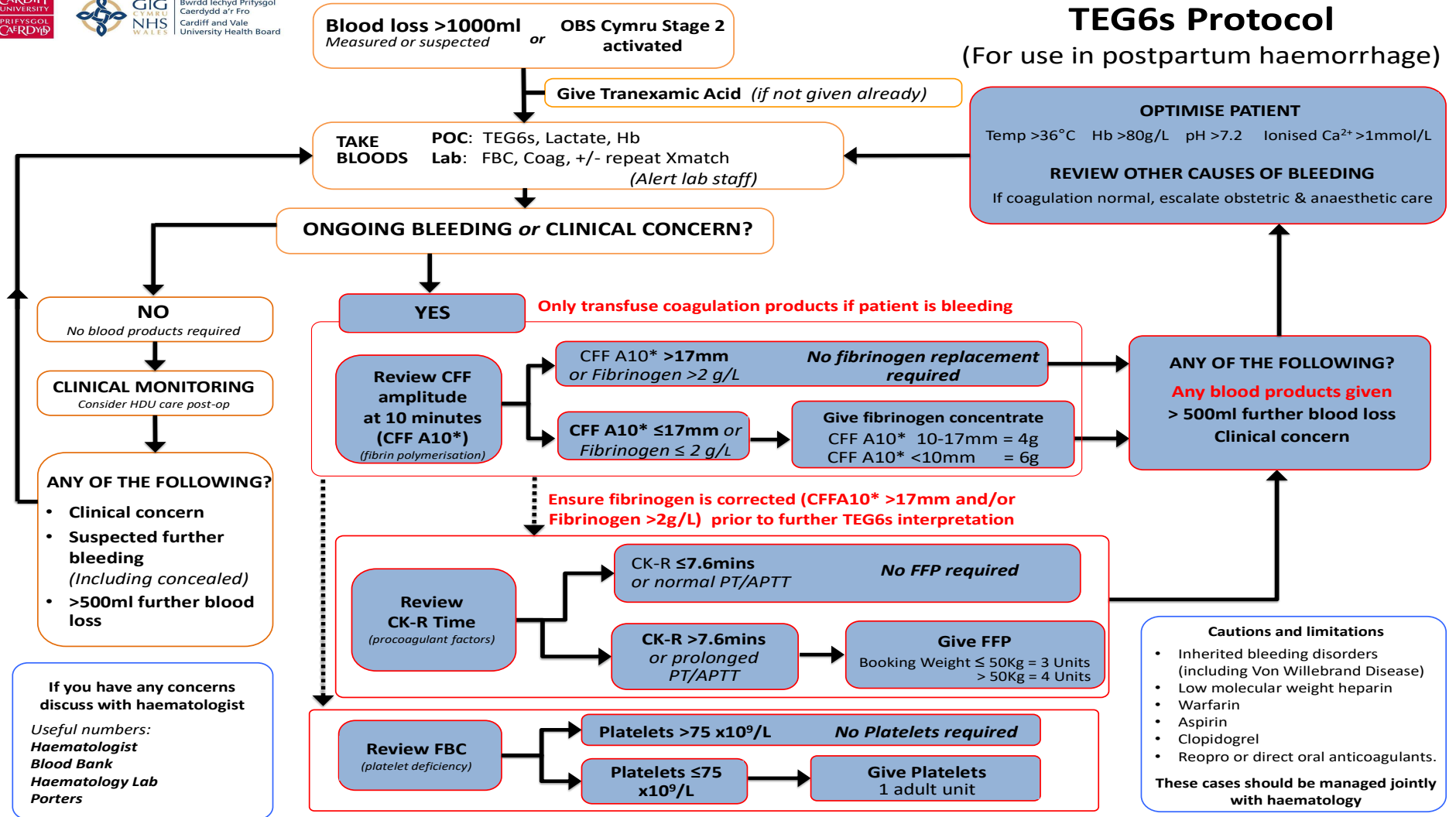
ROTEM Protocol

(For use in postpartum haemorrhage)



TEG6s Protocol

(For use in postpartum haemorrhage)

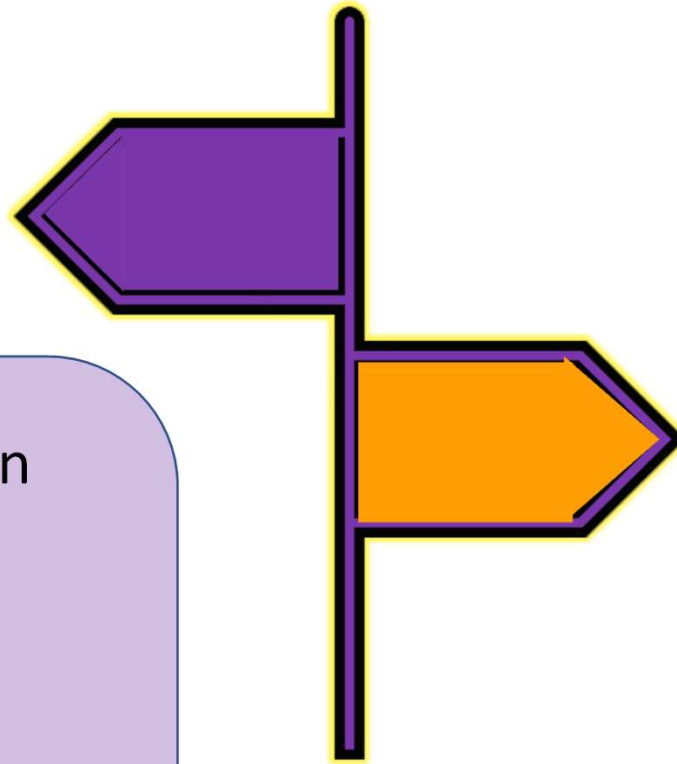


No Coagulopathy

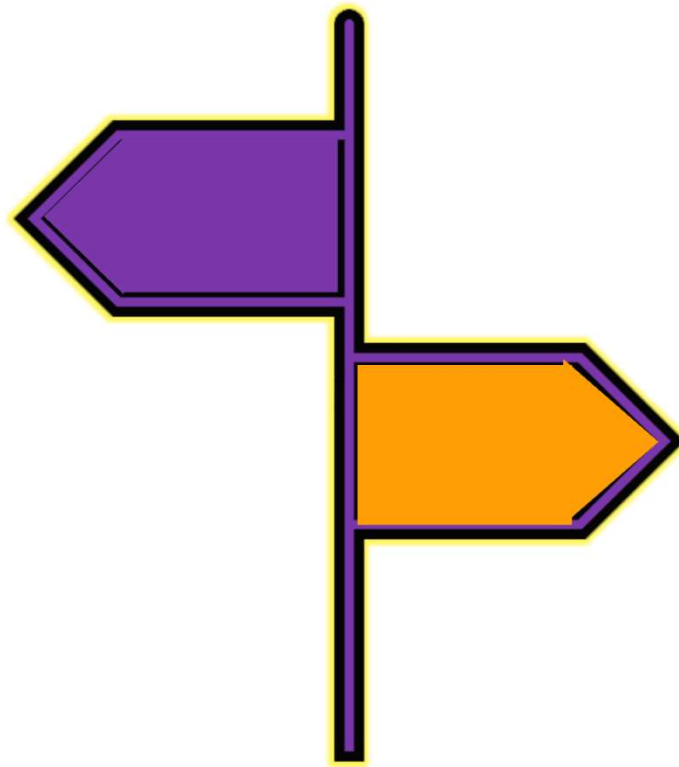
Withhold coagulation products

Treat cause
- trauma, tone, tissue

Repeat + 500ml
& track coagulation



VHA TESTS



VHA TESTS

Coagulopathy

Replace Fibrinogen $>2\text{g/L}$

Repeat test ensure adequacy

Treat cause

- trauma, tone, tissue

+/- FFP



Impact

- Timely appropriate treatment
- Reduced progression
- Reduced blood product transfusion
- Reduced Iatrogenic injury

Liverpool data- reduced total units transfused

OBS Cymru- reduced RBC transfusion

McNamara H, Kenyon C, Smith R, Mallaiah S, Barclay P. Four years' experience of a ROTEM[®]-guided algorithm for treatment of coagulopathy in obstetric haemorrhage. *Anaesthesia*. 2019 Aug;74(8):984-991. doi: 10.1111/anae.14628. Epub 2019 Apr 5. PMID: 30950521.

Bell SF et.al. Reduction in massive postpartum haemorrhage and red blood cell transfusion during a national quality improvement project, Obstetric Bleeding Strategy for Wales, OBS Cymru: an observational study. *BMC Pregnancy and Childbirth* volume 21, Article number: 377 (2021)

Limitations of VHA in PPH

Anticoagulant therapy

Inherited bleeding disorders

Sepsis coagulopathy (sepsis DIC)

Potentials

- Identify and correct hypofibrinogenaemia
- Avoid unnecessary blood products
- Personalise PPH care
- Improve outcomes in PPH

Thank you

PPH algorithms for ROTEM Sigma and TEG6s
for Cryoprecipitate and Fibrinogen concentrate
will be available shortly on the new OAA Website