BLEEDING MANAGEMENT IN POSTPARTUM HEMORRHAGE

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Overview

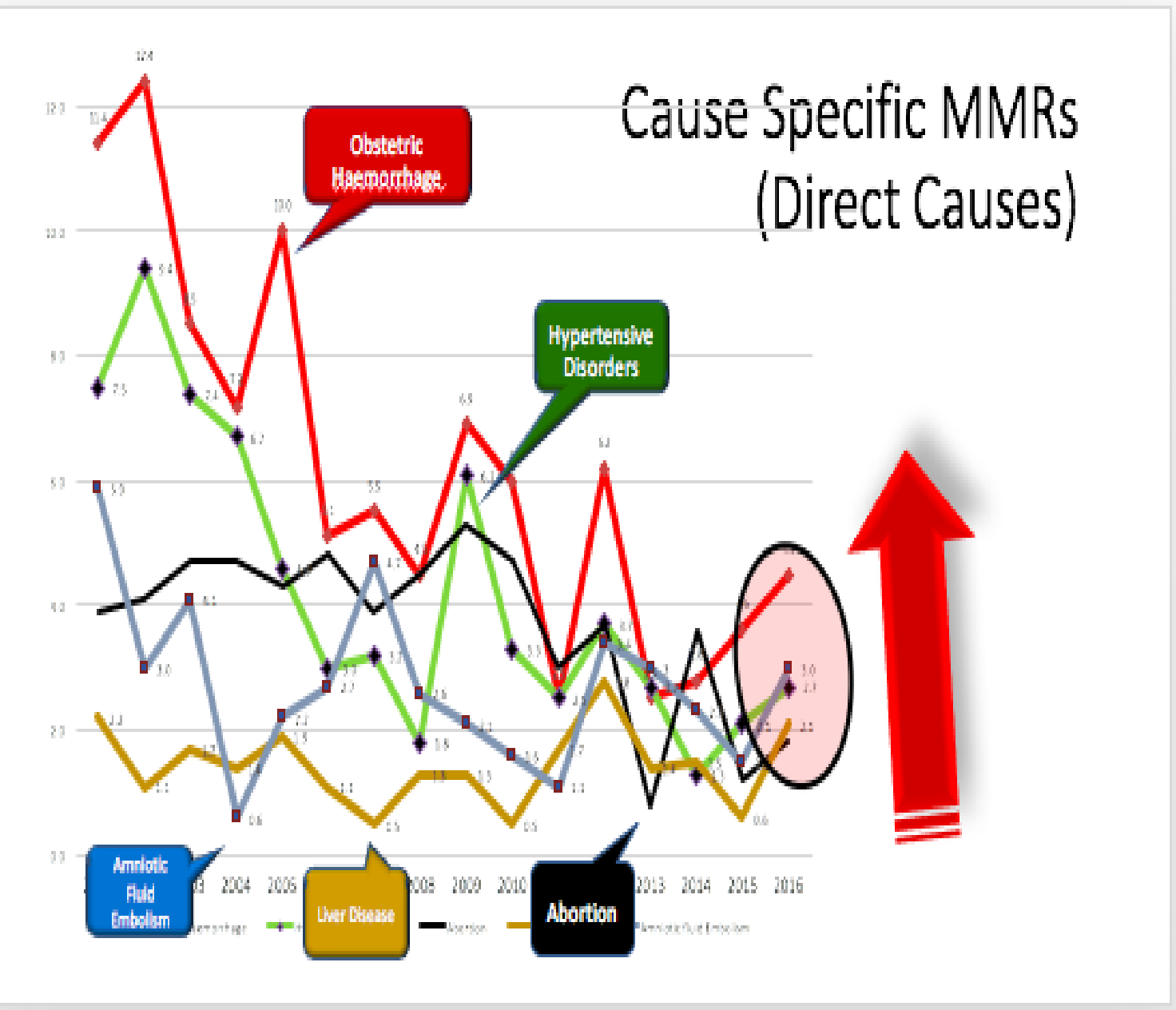
- Clinical burden of PPH
- Basics of PPH
- Approach to manage bleeding
- Medical management
- Our experience at CSHW

Post-partum Hemorrhage: Worldwide

- PPH rates 30-70/ 1000 births
- 69690 deaths in the year 2015
- Common in low resource settings

Global health estimates 2015 -WHO

PPH in Sri Lanka



- Number one cause of maternal deaths 2016
  - 13.3% of total deaths
- 68% of maternal severe morbidity 2016

National Maternal Mortality Reviews

Maternal mortality - Sri Lanka

- **Lowest in the South Asian region**
- **39/100000 live births in 2017 : 60% are preventable**

India 130/100000(2016-2017)

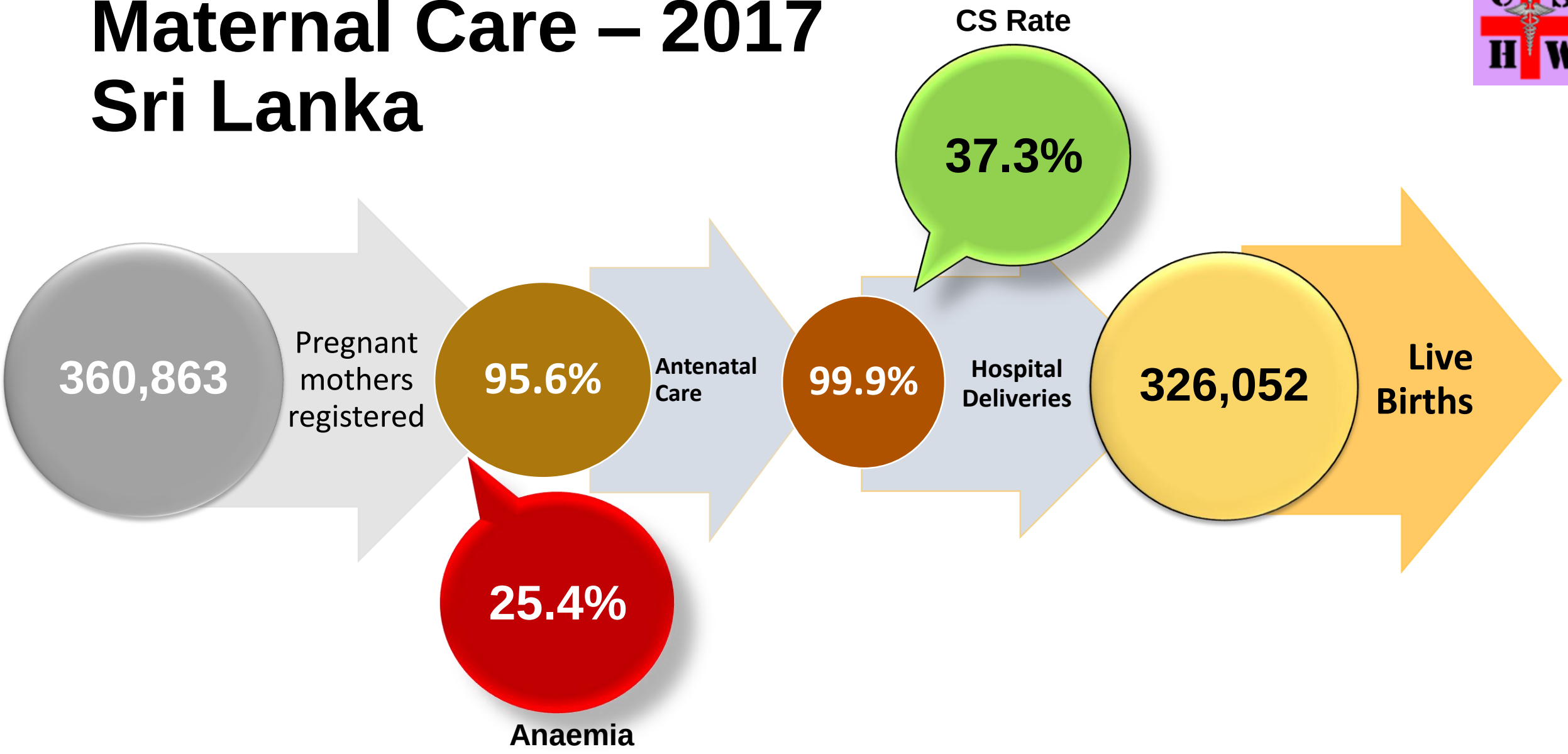
Pakistan 178/100000(2015)

Family Health Bureau- Ministry of Health

National Maternal Mortality Reviews – 2017

Outcome Dissemination

Maternal Care – 2017
Sri Lanka



Definitions

PPH Loss of 500ml or more blood within 24 hours of delivery, irrespective of the mode of delivery.

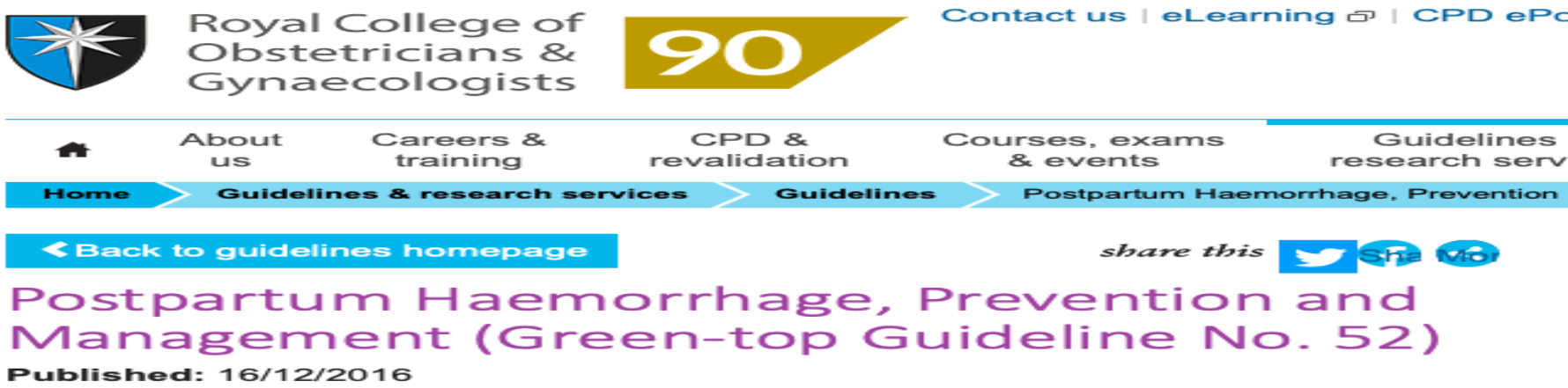
Grades **Minor** 500-1000ml

Major: **Moderate** 1000-2000ml + signs & symptoms

Severe > 2000ml, or hypovolaemic shock

acute loss of > 40% blood volume

rate > 130ml/min & ongoing



Physiological changes in Pregnancy

- Hypercoagulable state:
  Most clotting factors increase
  Serum fibrinogen increases by 150-200% (4-6 g/l)
- Fibrinolysis decreases
- Natural anticoagulant protein S decreases

- Blood volume increases by 50%
- Physiological anemia – Hb 10.5-11 g/dl

- Platelet count is in the lower range

Mechanisms of PPH

- **Tone**
- **Tissue**
- **Trauma**
- **Thrombin / Fibrinogen Combinations**

PPH : Clinical Presentation

- **Unanticipated sudden bleeding:**

60% Uterine atony, **no identifiable risk factor**

No time for planning.

Drills, Local guidelines are essential.

- **Anticipated bleeding**: Placenta accreta spectrum disorders (PAS)

Planning and optimal management is possible.

PPH
Approach to manage bleeding

- **Antenatal**

  Identification, optimization & planning delivery of high risk pregnant women
- **Intrapartum**

  Standard measures to minimize bleeding at delivery

  Specific measures according to the antenatal plan
- **Postpartum**

  Detect PPH early

  Manage bleeding according to severity

Antenatal Identification, Optimization & Planning

- **Anemia**

Hb < 11g/dl – *WHO definition of anemia in pregnancy.*

- Potential risk of PPH
- **Postpartum anemia**

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Alexandria University Faculty of Medicine
Alexandria Journal of Medicine
http://www.elsevier.com/locate/ajme

Postpartum hemorrhage is related to the hemoglobin levels at labor: Observational study

5. Conclusion

The finding of this study support the link between low hemoglobin levels at delivery and the potential risk of PPH which remains currently debated. Also we provide evidence of the association between severe anemia and severe uterine atony requiring emergency hysterectomy.

Corrective measure

Antenatal Iron therapy

Identify pregnant women at high risk of PPH

- **Placenta accreta spectrum disorders:** increasing with rising CS rates
- Obstetric complications: HELLP, AFLP, AFE, IUD
- Medical complications: Dengue fever
- Women on anticoagulants/antiplatelet drugs
- Large baby/ Twins

Preventive measures at 3rd stage of labour

Active management of the third stage of labour to prevent PPH (1A)

- Vaginal delivery: oxytocin (5 IU) intravenously (**1A**)

  10U IM WHO 2012

- Caesarean section: oxytocin (5 IU) intravenously (**1A**).
- Intravenous administration of tranexamic acid (0.5–1.0 g) should be considered in women at increased risk of PPH (**1C**)

NICE accredited
www.nice.org.uk/accreditation

Green-top Guideline No. 52

December 2016

BLOOD TRANSFUSION

Blood Transfus. 2019 Mar; 17(2): 112–136.
Published online 2019 Feb 6. doi: 10.2450/2019.0245-18
PMCID: PMC6476742
PMID: 30865585

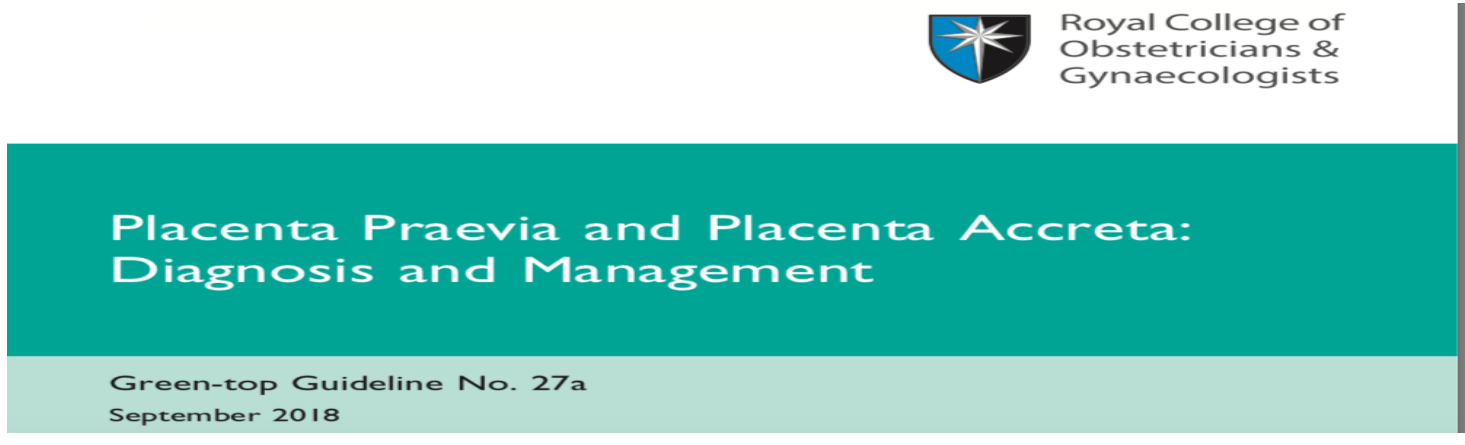
Patient blood management in obstetrics: prevention and treatment of postpartum haemorrhage. A NATA consensus statement

Specific measures
Placenta previa after caesarean section care bundle

The six elements considered to be reflective of good care are:

- Consultant obstetrician planning and directly supervising delivery.
- Consultant anaesthetist planning and directly supervising anaesthesia at delivery.
- Blood and blood products available.
- Multidisciplinary involvement in preoperative planning.
- Discussion and consent, including possible interventions (such as hysterectomy, leaving the placenta in situ, cell salvage and interventional radiology).
- Local availability of a level 2 critical care bed.

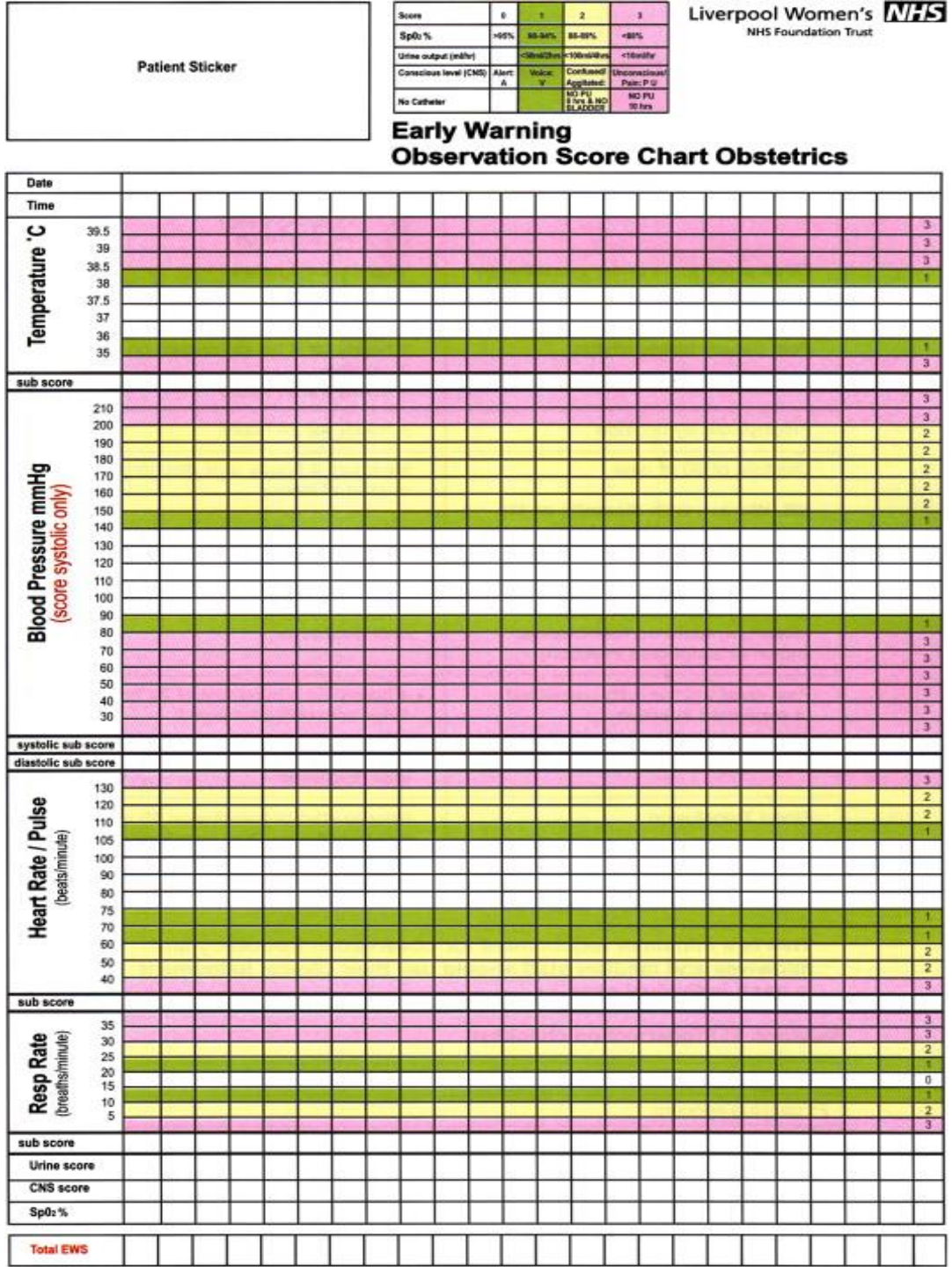
National safety agency & RCOG



Early detection of PPH
Track-Trigger-Response system: MEOWS

Facilitates

- early identification & prevention of maternal collapse
- early intervention with multidisciplinary input



TRACK & TRIGGER

White = 0 points

Green = 1 point

Yellow= 2 points

Pink = 3 points

3 in single parameter

Or > 5 total score = Moderate risk

> 7 total score = high risk

Need frequent monitoring every 3-5 min

&

Immediate assessment and treatment by R/SR/VOG

+

Anaesthetist

Major Hemorrhage & ongoing bleeding:

A life threatening emergency: Needs immediate action

Essential steps to be taken simultaneously to prevent lethal triad (Dilution coagulopathy hypothermia and acidosis)

- Resuscitate: ABCDE
- Call for help/Communicate, Multi disciplinary input
- Monitor: including IBP,CVP,CO
- Control bleeding: **Medical & Mechanical/Surgical**
- Stop or minimize factors contributing to bleeding

Based on data collected by the Royal College of Midwives the incidence of major obstetric haemorrhage is 3.7 per 1000 births and is still recognised as one of the leading causes of maternal death (RCM 2012), with no significant reductions in the UK death rate since 2009 (Merrifield 2016).

Components of medical control - major PPH

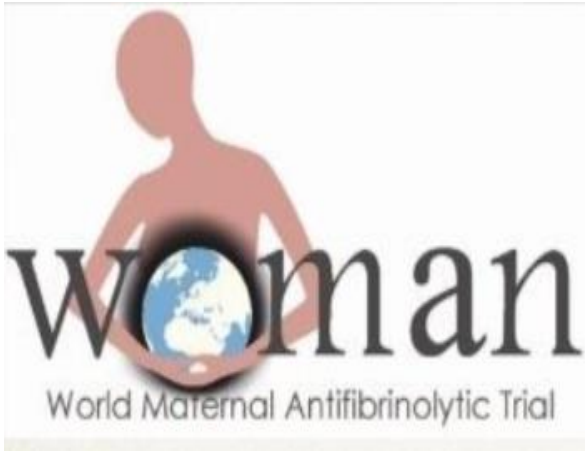
- Uterotonics
- Fibrinolytics
- Rapid replacement of deficit & ongoing loss to maintain CVS stability / organ perfusion : (Hypotensive resuscitation recommended by NATA)
  - Rapid blood transfusion to match rate of loss
  - Replace blood components
    - Avoid dilution
    - Avoid overload
- Minimize hypothermia, Metabolic acidosis

Therapeutic Uterotonics

- First-line oxytocin infusion 2-10 u/hour
- Second-line
  - ergometrine (0.2-0.5 mg, IM)
  - misoprostol (800 µg, sublingual), or
  - sulprostone (500 µg/1 hour, IV), or
  - carboprost (0.25 mg/15 min IM, up to 8 doses) (**1B**)

NATA consensus statement 2019, Green top guideline RCOG 2016

Tranexamic Acid



BLOOD TRANSFUSION

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Patient blood management in obstetrics: prevention and treatment of postpartum haemorrhage. A NATA consensus statement

- Recommendation 31. We recommend the administration of tranexamic acid (1 g by intravenous route) as soon as possible within the first 3 hours after PPH onset. This dose can be repeated after 30 min if bleeding continues (**1B**).

were randomly assigned to receive 1 g intravenous tranexamic acid (with a second dose given after 30 min, if needed) or placebo. Although the diagnosis was clinical, investigators specified that diagnosis of primary PPH could be based on clinically estimated blood loss of more than 500 mL after vaginal birth or 1,000 mL after caesarean section or any blood loss sufficient to compromise haemodynamic stability. Death due to bleeding was significantly reduced in women given tranexamic acid compared with placebo (1.5 *vs* 1.9%; p=0.045), especially in women treated within three hours of giving birth. There were no between-group differences in all other causes of death, hysterectomy rates or the incidence of adverse events (including thromboembolic events)[95]. Analysis of

Replacing blood in severe hemorrhage

- Restrict crystalloid (1-2 ml for each ml blood loss initially)
- Replace blood loss with blood as soon as possible
- Rapid transfusion of warmed blood via rapid warmer infuser O negative --> Group specific un-crossmatched--> crossmatched
- Intraoperative cell salvage: recommended

Blood Transfus. 2019 Mar; 17(2): 112–136. PMCID: PMC6476742
Published online 2019 Feb 6. doi: 10.2450/2019.0245-18 PMID: 30865585

Patient blood management in obstetrics: prevention and treatment of postpartum haemorrhage. A NATA consensus statement

Blood component replacement - an integral part of the management

Essential when uterotonics Tranexamic Acid blood & stitches fail

Formula driven vs Targeted therapy

Methods of replacing blood components

1. Empirical formula driven: Massive transfusion protocol/ shock packs
2. Early targeted therapy using POC TEM
3. Combination of 1 & 2

Is there a role for near patient testing of coagulation?

Green-top Guideline No. 47
May 2015

Centres that are using thromboelastography (TEG®, Haemonetics, Braintree, Massachusetts, USA) or rotation thromboelastometry (ROTEM®, Tem, Munich, Germany) for guiding blood transfusion during major obstetric haemorrhage must ensure that their transfusion algorithm protocol has been validated and that quality assurance measures are followed.

D

- **Recommendation 35**. We recommend assessing haemostatic competence and risk of coagulopathy in severe ongoing PPH through laboratory tests (platelet count, PT, international normalised ratio [INR], aPTT, fibrinogen level) or viscoelastic haemostatic tests to guide appropriate, goal-directed use of haemostatic blood components and pro-haemostatic agents (**1B**).

NATA consensus statement 2019

Guideline | Free Access

The use of viscoelastic haemostatic assays in the management of major bleeding

A British Society for Haematology Guideline

Recommendations

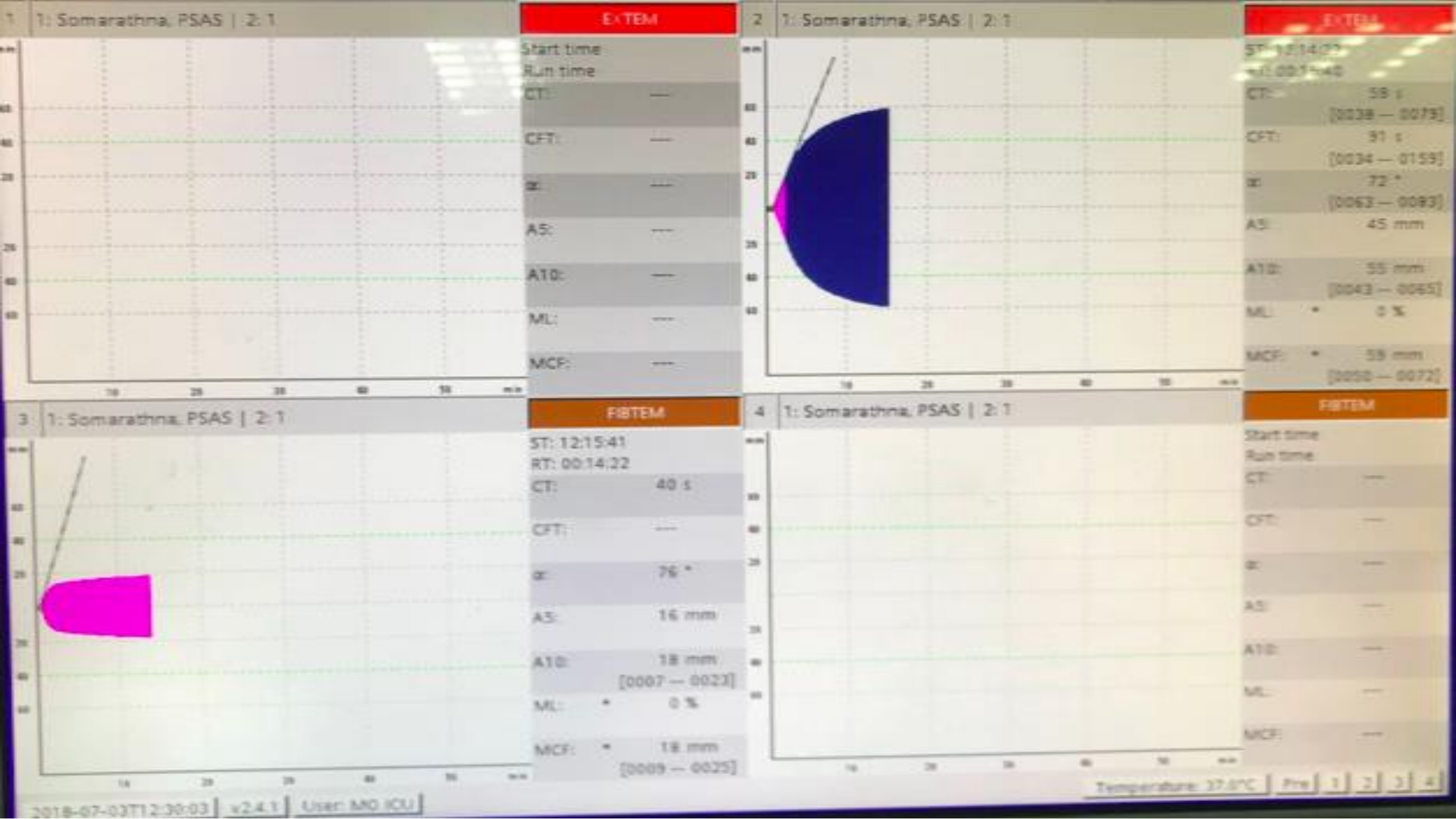
- **Viscoelastic haemostatic assays (VHA) are not usually helpful for predicting post-partum haemorrhage when taken during labour in a non-bleeding pregnant woman. Grade 2C.**
- **VHA may be used as part of an agreed algorithm to manage postpartum haemorrhage when the local institution's major obstetric haemorrhage protocol is activated. Grade 2C.**
- **During ongoing major postpartum haemorrhage, if the FIBTEM A5 is >12 mm fibrinogen replacement is unlikely to improve clinical haemostasis. Grade 2B.**
- **During major postpartum haemorrhage, if FIBTEM A5 is <7 mm, or <12 mm with ongoing bleeding, fibrinogen replacement may improve clinical haemostasis. Grade 2C.**
- **In a bleeding pregnant or post-partum patient, tranexamic acid should not be withheld based on the thromboelastography (TEG) or thromboelastometry (ROTEM)parameters. Grade 1B.**

EMPIRICAL FORMULA DRIVEN VS EARLY TARGETED THERAPY

	Formula driven therapy	Early targeted therapy
1. Basic concept	• Blood has RBC plasma & platelets: Replace all • Taken from Trauma & military practice **Given to all in similar manner without waiting for laboratory reports** **S pack 1 Blood : FFP : PLT 1:1:1** **S pack 2 Blood : FFP : PLT + Cryo 8-10 u**	• Find specific derangement using POC TEM. • Replace only the deficient factors: Usually fibrinogen Transfusion is **tailored to the patient's need**

EMPIRICAL FORMULA DRIVEN VS EARLY TARGETED THERAPY

	Formula driven therapy	Early targeted therapy
2. Tests guiding therapy	• **INR, APPT S Fibrinogen Platelet count** • Turnaround time > 90 min • Only numbers • Lab reference range for pregnant women not known • Indicates clotting derangement at the time of sampling **but correction is done > 1 ½ hours later – correct dose unknown.**	• **TEM @POC**; FibTEM ExTEM • Results in < 10 min • Numbers and graphical display - shows aspects of haemostasis that are difficult to obtain with traditional tests. • Validated for pregnant women • **Rapid correction can be done immediately and with the correct dose.**


1: Somarathna, PSAS | 2: 1
EXTEM
Start time
Run time
CT:
CFT:
α:
A5:
A10:
ML:
MCF:
2: 1
FIBTEM
ST: 12:15:41
RT: 00:14:22
CT: 40 s
CFT: ---
α: 76 °
A5: 16 mm
A10: 18 mm
[0007 — 0023]
ML: * 0 %
MCF: * 18 mm
[0009 — 0025]
Temperature: 37.0°C
Pre
1
2
3
4
2018-07-03T12:30:03
v2.4.1
User: IMO ICU

EMPIRICAL FORMULA DRIVEN VS EARLY TARGETED THERAPY

	Formula driven therapy	Early targeted therapy
3. Assessing the adequacy of replacement	• **Difficult :** need to wait for another >90 min	• **Very easy** : Validated dose calculation chart indicates the dose/Kg body weight Repeat test results in 10 min

What is Coagulopathy in PPH ?

Mainly depletion of fibrinogen over other coagulation factors

Early stage

- **Loss, Dilution and Deactivation**

Late stage

- **Consumption** (DIC)

British Journal of Anaesthesia **109** (6): 851–63 (2012)
Advance Access publication 16 October 2012 · doi:10.1093/bja/aes361

BJA

CME

Haemostatic monitoring during postpartum haemorrhage and implications for management

C. Solomon[1]*, R. E. Collis[2] and P. W. Collins[3]

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[2] Department of Anaesthesia, University Hospital of Wales, Cardiff, UK
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Predominant type of coagulopathy is dependent on etiology

DIC (consumption) appears early

Placental abruption, Dead fetus syndrome, Amniotic fluid embolism

Loss, dilution and deactivation

Ruptured uterus
Atonic uterus
Trauma
Retained products
Placental adhesive disorders

International Journal of Obstetric Anesthesia (2018) 33, 4–7
0959-289X/$ - see front matter © 2017 Published by Elsevier Ltd.
https://doi.org/10.1016/j.ijoa.2017.08.008

EDITORIAL

ELSEVIER
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How to replace fibrinogen in postpartum haemorrhage situations? (Hint: Don't use FFP!)

It is important to know the levels of serum fibrinogen early in haemorrhage

Why?

- **The first factor to drop precipitously is fibrinogen.**
- **An early biomarker for the progression of PPH**

  For each 1g/l drop, 2.63 fold increased risk for PPH

  When < 2g/l : 100% positive predictive value for severe PPH

  When > 4g/l : 79% negative predictive value for PPH

International Journal of Obstetric Anesthesia (2018) **33**, 4–7
0959-289X/$ - see front matter © 2017 Published by Elsevier Ltd.
https://doi.org/10.1016/j.ijoa.2017.08.008

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EDITORIAL

How to replace fibrinogen in postpartum haemorrhage situations? (Hint: Don't use FFP!)

What would be the rational treatment?

Replace fibrinogen rapidly

- Preemptive Fibrinogen therapy – not recommended
- Fibrinogen level not known & ongoing bleeding –

Replacement could be beneficial

Dose cannot be calculated

British Journal of Anaesthesia **114** (4): 623–33 (2015)
Advance Access publication 13 January 2015 · doi:10.1093/bja/aeu444

BJA

Pre-emptive treatment with fibrinogen concentrate for postpartum haemorrhage: randomized controlled trial†

A. J. Wikkelsø[1*], H. M. Edwards[2], A. Afshari[3], J. Stensballe[4], J. Langhoff-Roos[5], C. Albrechtsen[3], K. Ekelund[3], G. Hanke[3], E. L. Secher[3], H. F. Sharif[5], L. M. Pedersen[6], A. Troelstrup[6], J. Lauenborg[7], A. U. Mitchell[1], L. Fuhrmann[1], J. Svare[2], M. G. Madsen[8], B. Bødker[9], A. M. Møller[1] and FIB-PPH trial group

Conclusions. We found no evidence for the use of 2 g fibrinogen concentrate as pre-emptive treatment for severe PPH in patients with normofibrinogenaemia.

Rapid correction of fibrinogen level

Important steps to follow

- Rapid blood loss or >1000ml - commence rapid warm blood transfusion.
- Do POC TEM test : FibTEM A5, ExTEM
- Look at the graph (TEMogram) width and the test result

  FibTem A5 > 12mm is normal, < 12mm is abnormal
- Check the deficit in mm to bring it up to 12 mm
- Calculate the dose using the validated table & transfuse immediately
- What is the source of fibrinogen?

  FFP : Need a large volume (has little fibrinogen)

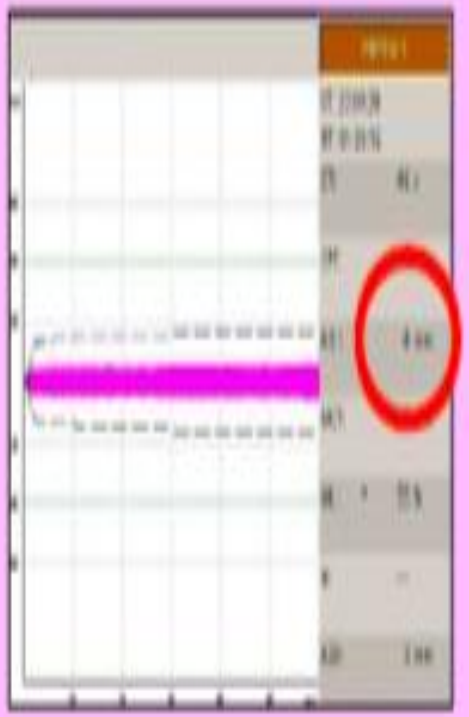
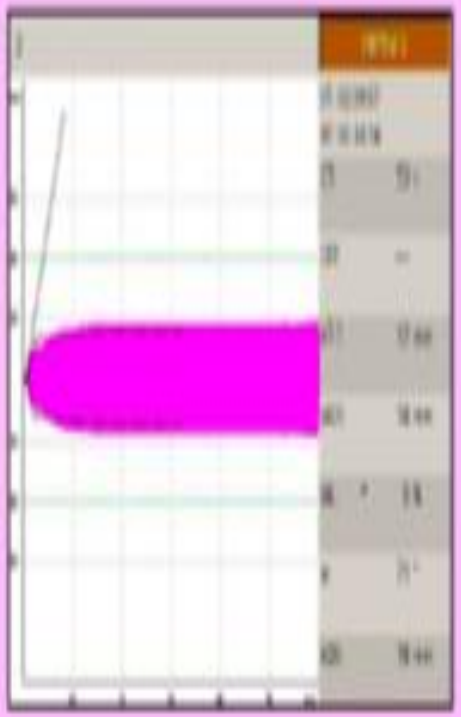
  Cryoprecipitate: small volume (has up to 20 times that of FFP)

  Fibrinogen concentrate : the best, no preparation time

A plasma fibrinogen level of greater than 2 g/l should be maintained during ongoing PPH. [*New 2016*] C

Cryoprecipitate should be used for fibrinogen replacement. [*New 2016*] Green top guideline 2016 D

RAPID CORRECTION OF FIBRINOGEN LEVEL

	ABNORMAL ROTEM	CRITERIA	DIAGNOSIS	INTERVENTION	CORRECTED ROTEM
FIBRINOGEN		Is **FIBTEM A5 ≤12mm**?	**Low fibrinogen**	**Cryoprecipitate OR fibrinogen concentrate** (see fibrinogen dosing guide overleaf) Consider **tranexamic acid** 1g IV	

STUDY at CSHW

Retrospective, observational, single center study
over a period of 4 years

OBJECTIVES

Assess whether early targeted therapy using POC TEM compared to empirical formula driven treatment has

- made any improvements in outcomes
- made any benefits to the health care system

Findings

- 86% increase in cryoprecipitate transfusion. **P : 0.000**
- 32% of patients in the TEM group did not need cryoprecipitate despite having a major bleed
- 45% reduction of platelet transfusions with TEM group. **P : 0.025**
- 73% reduction in FFP transfusion in TEM group **P : 0.000**
- 48% reduction in the blood product volume transfused **P : 0.0253**

Findings

- No significant reduction of blood volume transfused - 7% decrease P 0.5
- No significant reduction in blood loss- P 0.9
- A 10. 1 % reduction in hysterectomy rate
- Over all lesser percentages of complications: TACO (P < 0.008)
- ICU stay - 45% reduction with TEM group **P : 0.000**
- 28 % reduction in total expenditure

CONCLUSIONS

- Early targeted therapy is associated with
  - fewer blood component transfusions
  - fewer complications associated with those transfusions
  - shorter ICU stay
  - lower cost.
- The study suggested that early targeted therapy would be the better method in replacing blood components in the future management of PPH

Retrospective analysis of 51 cases of PPH managed with ROTEM guided blood component replacement over a period of 18 months (Jan 2018 - June 2019)

Hysterectomy Rate (%)	17.6						
Average ICU Stay (days)	2.0						
Mode of Anaesthesia Used	SAB	GA	Labour Epidural Topup	CSE			
% of patients	80.4	11.8	2.0	5.9			
Blood Product Use	FFP	Cryo	Platelets				
% of patients	7.8	52.9	13.7				
Average Number of Bags	4.3	29.0	5.4				
Average No. of Units of Blood Given	3.7						
Average Blood Loss (ml)	2078.4						
Cause of Bleeding	Placenta Accreta Spectrum	Atony	Placenta Praevia	Trauma			
% of patients	74.5	11.8	11.8	3.9			
Frequency of Complications (%)	19.6						
Complications	Increase CRP	Reaction to Cryo	Paralytic Ileus	Hematuria	Reopening	Transfusion Reaction	AKI/HELLP
% of patients	3.9	2.0	5.9	3.9	2.0	2.0	2.0

Current situation at CSHW

- Cause of PPH – 75% due to PAS disorders
- Aim for uterus preserving surgery (low hysterectomy rates 17.6%)
- 80% of cases are done under spinal anesthesia
- Essential equipment available : Rapid warmer infuser, invasive monitoring, Patient warmers
- POC TEM-guided protocol is used for all cases
- Morbidity – minimal & Mortality - 0

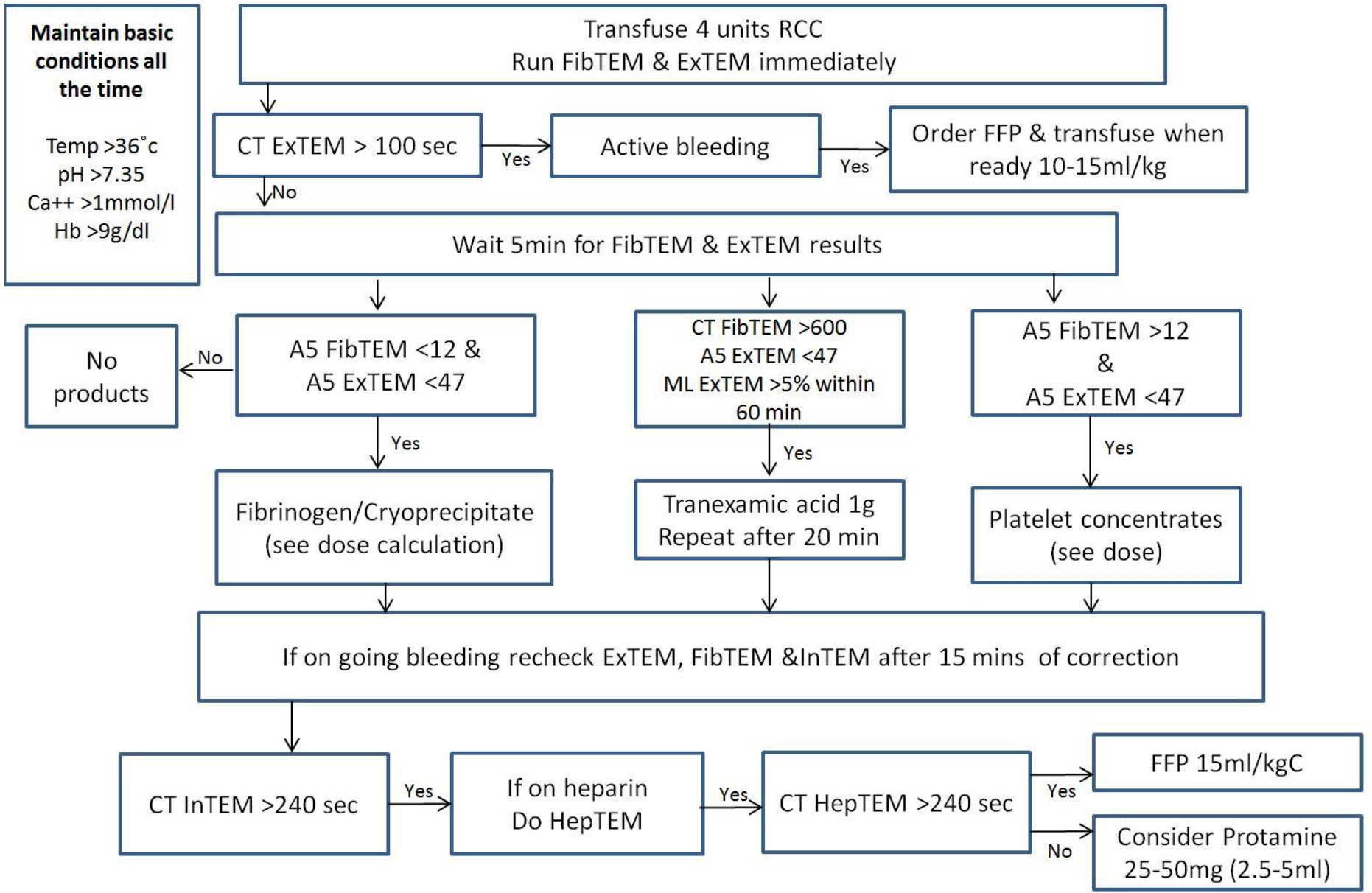
The journey to success:
Our story

- Purchased the ROTEM delta machine locally in 2014 - cost Rs 4 million (~USD 22000)
- Installed it in our ICU: only machine available at point of care in Sri Lanka. Other machines are not available at point of care
- The company began running information sessions regularly for ICU staff, and several times later on request.

Journey to success....

- Initially followed Liverpool Women's Hospital's algorithm
- Later modified it with the evidence based algorithm & validated dose calculation chart of Dr Klaus Gorlinger (a pioneer anaesthetist UH Essen, Germany)
- It is easy to follow the algorithm and correct hemostatic defects with little required experience

Management of massive obstetric haemorrhage- blood loss >40% blood volume (Blood volume calculated as 100ml/kg) Guided by results from ROTEM-CSHW



Fibrinogen/Cryoprecipitate dose

Target increase in A5 FibTEM (mm)	Fibrinogen mg/kg BW	Cryoprecipitate (ml/kg)/ units
2	12.5	1ml/kg(5u)
4	25	2ml/kg(10u)
6	37.5	3ml/kg(15u)
8	50	4ml/kg(20u)
10	62.5	5ml/kg(25u)
12	75	6ml/kg(30u)

Platelet dose

A5 ExTEM	Dose
<35mm	4 units platelets
<25mm	8 units platelets
<15mm	8 units platelets + Cryo

Ref : Dr Klaus Görlinger A5 algorithm and LWH UK protocol

Management of massive haemorrhage in Obstetrics CSHW

More than 40% of blood volume (100ml/kg) and on-going severe bleeding.
Collapse/shock.

Activate massive haemorrhage pathway (Inform registrar, senior registrar and consultant in obstetrics)

STOP THE BLEEDING

Haemorrhage control
Bimanual compression.
Ergometrine 500 µg im
Syntocinon 40 IU infusion (10 u/h)
Check placenta and for trauma
Misoprostol 800 µg rectal/SL
Tranexamic acid 1g iv ,repeat after 20 min
EUA and BalloonTamponade
Compression sutures
Hysterectomy +/- Bilateral internal iliac artery ligation

Always warm patient and fluid/blood.
Consider Calcium gluconate

Move the stable patient to ICU.

Call for help.
Inform anaesthesia registrar, consultant anaesthetist..

RESUSCITATE
ABCDE AND MONITOR

Take blood and send to lab. Inform blood bank.
FBC,INR,APTT, fibrinogen, U+E, calcium
ABG,ROTEM. Send samples to ICU.
Order MHP 1

Order red cells 4 units. Cryoprecipitate 20 units. Platelets 1 AD. Follow ROTEM pathway.

OR

No ROTEM?
Order red cells 4 units.
FFP 4 units
Platelets 1 (adult D)
And give 4:4:1 + cryo 10u

Suspected or continuing haemorrhage requiring further transfusion:
REASSESS consider arterial and central venous lines.
REPEAT ROTEM and correct according to pathway.
If no ROTEM order MHP2 (RBC 4u, FFP 4u, Platelet1AD, cryo 20u) and transfuse.
If further bleeding occurs contact haematologist/transfusion medicine specialist.

Repeat investigations including ROTEM.

Aims for therapy:
Hb 9-10g/dL
Platelets >75x10^9/L, ExTem A5> 47
INR & APTTI <1.5,ExTem CT <100
Fibrinogen >3 g/L, FibTem A5 >12
Ca2+ >1mmol ML ExTem <5%
Temp >36˚C within 60min
pH >7.35
K+ 3.8-5mmol/l

STAND DOWN
Return unused components.
Document.

The journey to success …..

- Mentors were identified, with those who had shown special interest being allowed to educate and run tests in difficult circumstances.
- TEM guided coagulation management is a team effort.
- Every member has a responsibility that they need to be aware of.

Summary

- 50-60 % of PPH deaths are preventable
- No pregnant woman should die of PPH in the modern practice of medicine
- Clinicians have a major role to play by practicing the evidence based approach


Thank You