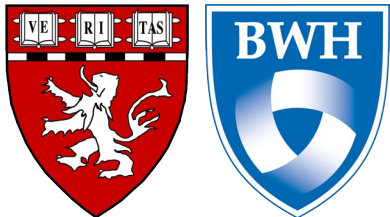


Postpartum Hemorrhage: An Update

SFOAI 2024

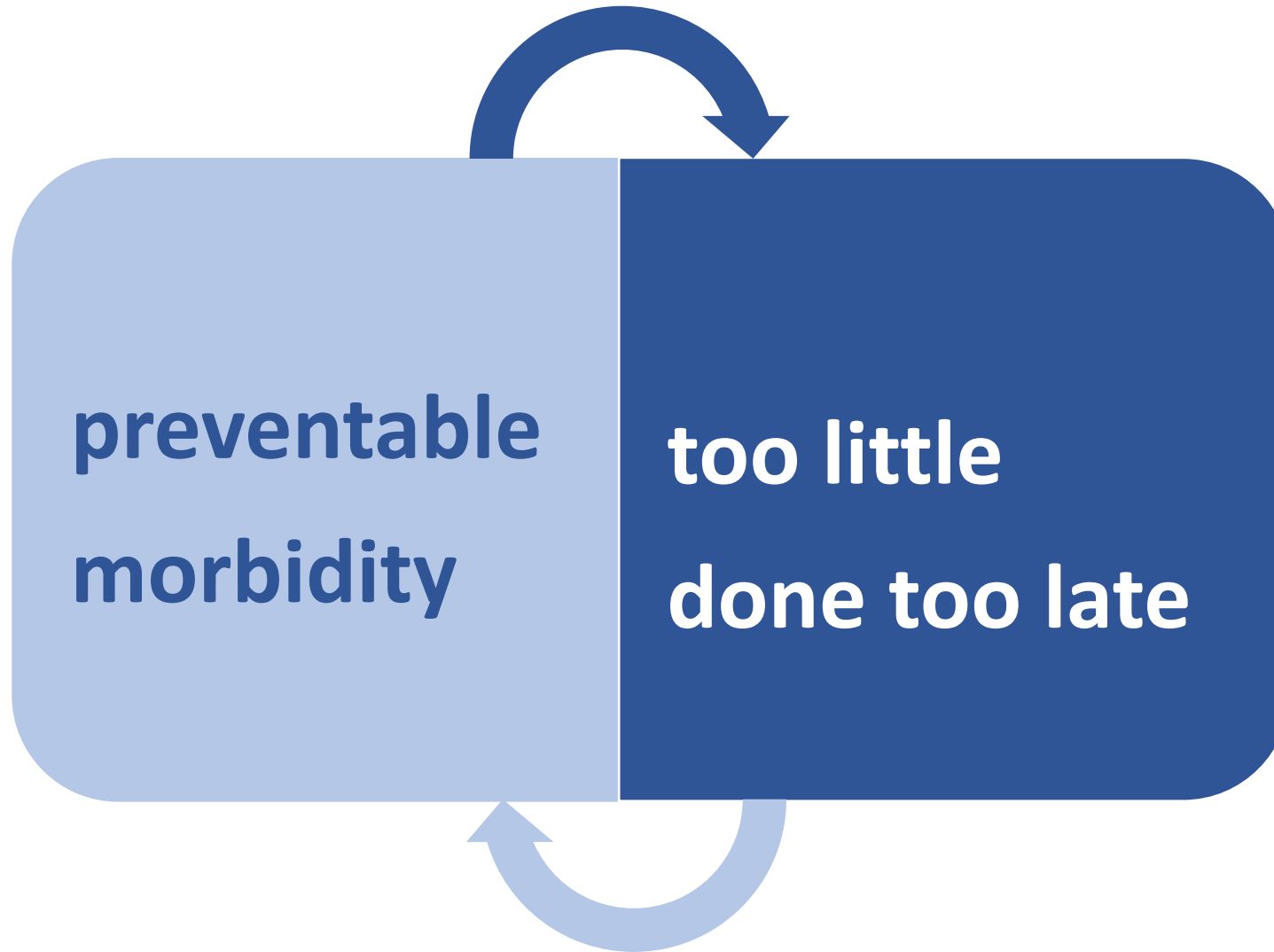
Happy Tammsvik, Sweden

Michaela K. Farber MD MS
Associate Professor, Harvard Medical School
Division Chief, Obstetric Anesthesia
Brigham and Women's Hospital
Boston, MA



SFOAI

Postpartum Hemorrhage: the leading cause of **preventable morbidity**



Objectives: Postpartum Hemorrhage

- **Optimize** your unit policies overall, with focus on risk assessment and early detection
- **Recognize** the latest evidence for pharmacologic treatment modalities
- **Integrate** an up-to-date, impactful obstetric hemorrhage protocol



Objectives: Postpartum Hemorrhage

- **Optimize your Unit Polices**
 - **Assess Hemorrhage Risk**
 - **Detect Hemorrhage Early**



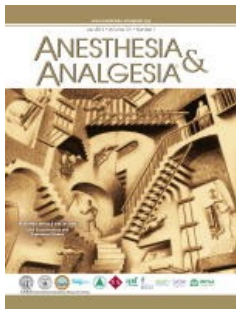
National Partnership for Maternal Safety: Consensus Bundle on Obstetric Hemorrhage

Elliott K. Main, MD, Dena Goffman, MD, Barbara M. Scavone, MD, Lisa Kane Low, PhD, CNM, Debra Bingham, DrPH, RN, Patricia L. Fontaine, MD, MS, Jed B. Gorlin, MD, David C. Lagrew, MD, and Barbara S. Levy, MD

Hemorrhage is the most frequent cause of severe maternal morbidity and preventable maternal mortality and therefore is an ideal topic for the initial national maternity patient safety bundle. These safety bundles outline critical clinical practices that should be implemented in every maternity unit. They are developed by multidisciplinary work groups of the National Partnership for Maternal Safety under the guidance of the Council on Patient Safety in Women's Health Care. The safety bundle is organized into four domains: Readiness, Recognition and Prevention, Response, and Reporting and System Learning. Although the bundle components may be adapted to meet the resources available in individual facilities, standardization within an institution is strongly encouraged. References contain sample resources and "Potential Best Practices" to assist with implementation. (Anesth Analg 2015;121:142-8)

The National Partnership for Maternal Safety: A Call to Action for Anesthesiologists

Barbara M. Scavone, MD,* and Elliott K. Main, MD†



- **13 Key Elements**
- **4 Action Domains**
 - **Readiness**
 - **Recognition**
 - **Response**
 - **Reporting**

Box 1. Obstetric Hemorrhage Safety Bundle From the National Partnership for Maternal Safety, Council on Patient Safety in Women's Health Care

Readiness (Every Unit)

1. Hemorrhage cart with supplies, checklist, and instruction cards for intrauterine balloons and compression stitches
2. Immediate access to hemorrhage medications (kit or equivalent)
3. Establish a response team—who to call when help is needed (blood bank, advanced gynecologic surgery, other support and tertiary services)
4. Establish massive and emergency-release transfusion protocols (type-O negative or uncrossmatched)
5. Unit education on protocols, unit-based drills (with postdrill debriefs)

Recognition and Prevention (Every Patient)

6. Assessment of hemorrhage risk (prenatal, on admission, and at other appropriate times)
7. Measurement of cumulative blood loss (formal, as quantitative as possible)
8. Active management of the 3rd stage of labor (department-wide protocol)

Response (Every Hemorrhage)

9. Unit-standard, stage-based obstetric hemorrhage emergency management plan with checklists
10. Support program for patients, families, and staff for all significant hemorrhages

Reporting and Systems Learning (Every Unit)

11. Establish a culture of huddles for high-risk patients and postevent debriefs to identify successes and opportunities
12. Multidisciplinary review of serious hemorrhages for systems issues
13. Monitor outcomes and process metrics in perinatal quality improvement committee

<http://www.safehealthcareforeverywoman.org>

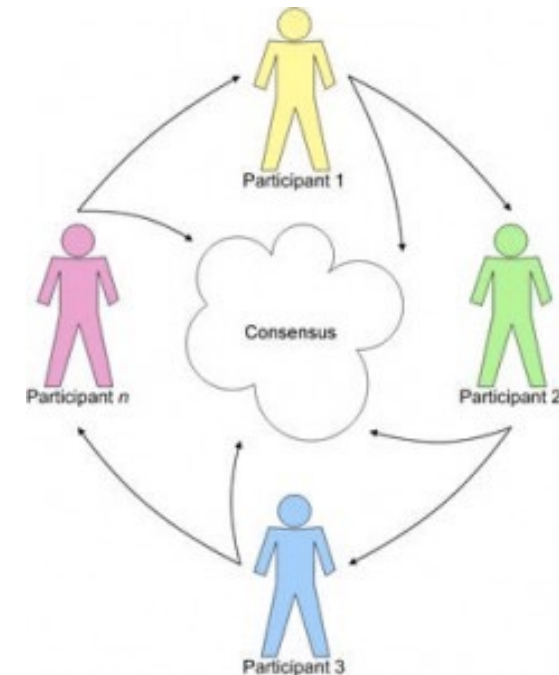
Identifying Barriers to Implementation of the National Partnership for Maternal Safety Obstetric Hemorrhage Bundle at a Tertiary Center: Utilization of the Delphi Method

Annemaria De Tina, MD, FRCPC,*† Anthony Chau, MD, MMSc, FRCPC,*‡
Daniela A. Carusi, MD, MSc,*§ Julian N. Robinson, MD,*§ Lawrence C. Tsen, MD,*
and Michaela K. Farber, MD, MS*

Delphi Technique

Steps to Establish Delphi Technique

1. Assemble a panel of experts.
2. Create a questionnaire of open-ended questions.
3. Summarize the responses and feed back to the panel until the members reach agreement.
4. Create a brief report and send to the panel members for agreement/disagreement.
5. Continue the feedback process until panel reaches agreement.



Delphi Method

- Four rounds
- All disciplines

Benefits

- Gathers consensus
- Reveals deficiencies
- Establishes buy-in
- Enhances dialogue

DELPHI SURVEY METHOD

ROUND 1

Do you think each component of the NPMS consensus bundle on OB hemorrhage is adequately implemented?
List and explain the barriers to implementation.



ROUND 2

Are you in **agreement/disagreement** with the barriers and recommended improvements proposed by your colleagues?
(≥60% agreement carried to rounds 3 and 4)



ROUND 3

Rank the feasibility of overcoming each barrier and implementing recommended improvements
Rank the impact of each on patient care.



ROUND 4

Are you in **agreement/disagreement** with barriers and recommended improvements proposed by the other disciplines?

Identifying Barriers to Implementation of the National Partnership for Maternal Safety Obstetric Hemorrhage Bundle at a Tertiary Center: Utilization of the Delphi Method

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and Michaela K. Farber, MD, MS*

At a busy tertiary center...

- Every bundle element was ranked as deficient by at least one person surveyed
- **Six of 13 (46%) of elements** were rated as deficient by consensus

KEY POINTS

- **Question:** What barriers exist to the implementation of the national partnership for maternal safety obstetric hemorrhage bundle?
- **Findings:** Six of the 13 bundle elements achieved multidisciplinary consensus as being deficient and were ranked for patient impact and implementation feasibility.
- **Meaning:** The Delphi method identifies institutional deficiencies and promotes tangible, meaningful, and multidisciplinary systemic improvements.

- **13 Key Elements**
- **4 Action Domains**
 - **Readiness**
 - **Recognition**
 - **Response**
 - **Reporting**

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Recognition and Prevention (Every Patient)

6. Assessment of hemorrhage risk (prenatal, on admission, and at other appropriate times)

possible)

8. Active management of the 3rd stage of labor (department-wide protocol)

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<http://www.safehealthcareforeverywoman.org>

Recognition and Prevention (Every Patient)

6. Assessment of hemorrhage risk (prenatal, on admission, and at other appropriate times)

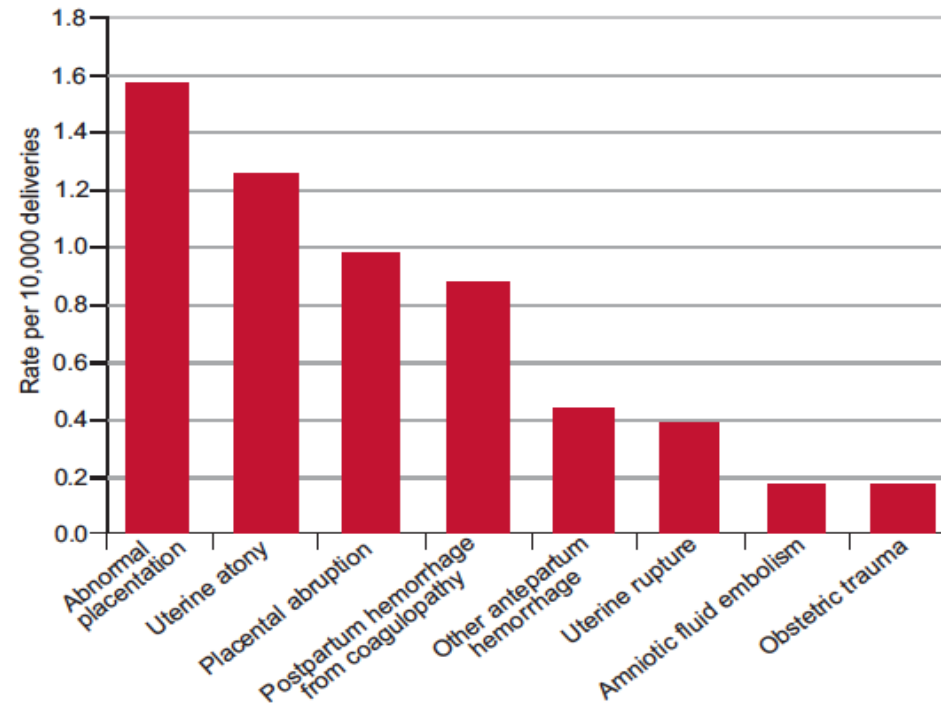
- System in place?

- High-risk patient clinics

- Risk assessment on admission

- Safety rounds

- Preoperative huddle



- Massive transfusion during hospitalization for delivery, NY state 1998-2007

Low Clot only	Medium Type and Screen	High Type and Crossmatch
No prior uterine surgery	Prior cesarean delivery or uterine surgery	Placenta previa
Singleton pregnancy	Multiple gestation	Suspected placenta accreta
No bleeding disorder	Chorioamnionitis	Known coagulopathy
≤ 4 prior vaginal births	>4 vaginal births	Hematocrit < 30 AND risk factors
No history of PPH	History of prior PPH	Platelets < 100,000
	Large fibroids	Active bleeding on admission



- Prolonged 2nd stage
- Prolonged oxytocin
- Active bleeding
- Chorioamnionitis
- Vacuum or forceps
- Emergency cesarean
- Retained placenta

Admission

Labor and Delivery

RISK CATEGORY: ADMISSION			
	Low Risk	Medium Risk (2 or More Medium Risk Factors Advance Patient to High Risk Status)	High Risk
	<input type="checkbox"/> No previous uterine incision	<input type="checkbox"/> Induction of labor (with oxytocin) or Cervical ripening	<input type="checkbox"/> Has 2 or More Medium Risk Factors
	<input type="checkbox"/> Singleton pregnancy	<input type="checkbox"/> Multiple gestation	<input type="checkbox"/> Active bleeding more than "bloody show"
	<input type="checkbox"/> ≤4 Previous vaginal births	<input type="checkbox"/> >4 Previous vaginal births	<input type="checkbox"/> Suspected placenta accreta or percreta
	<input type="checkbox"/> No known bleeding disorder	<input type="checkbox"/> Prior cesarean birth or prior uterine incision	<input type="checkbox"/> Placenta previa, low lying placenta
	<input type="checkbox"/> No history of PPH	<input type="checkbox"/> Large uterine fibroids	<input type="checkbox"/> Known coagulopathy
		<input type="checkbox"/> History of one previous PPH	<input type="checkbox"/> History of more than one previous PPH
		<input type="checkbox"/> Family history in first degree relatives who experienced PPH (known or unknown etiology with possible coagulopathy)	<input type="checkbox"/> Hematocrit <30 <u>AND</u> other risk factors
		<input type="checkbox"/> Chorioamnionitis	<input type="checkbox"/> Platelets <100,000/mm ³
		<input type="checkbox"/> Fetal demise	
		<input type="checkbox"/> Polyhydramnios	



= identical to CMQCC tool

Which tool to implement?

- ACOG, AWHONN, CMQCC
- Patients with PPH: up to 41% are “low risk” by such tools
- We need to refine our tools



Risk Factors for Atonic Postpartum Hemorrhage

A Systematic Review and Meta-analysis

Holly B. Ende, MD, M. James Lozada, DO, David H. Chestnut, MD, Sarah S. Osmundson, MD, MS, Rachel L. Walden, MLIS, Matthew S. Shotwell, PhD, and Jeanette R. Bauchat, MD, MS

- 27 studies reporting ≥ 1 risk factor for PPH
- 19 – qualitative data
- 13 – meta-analyzed
- 47 potential risk factors
- **15: definite or likely**

	Selection of participants	Confounding variables	Measurement of exposure	Blinding of outcome assessments	Incomplete outcome data	Selective outcome reporting	Summary risk of bias
Bateman (2010)	+	+	+	+	+	+	+
Bateman (2013)	+	+	+	+	+	+	+
Bekabil (2015)	+	X	+	X	+	+	X
Bryant (2012)	+	+	+	+	+	+	+
Callaghan (2010)	+	+	+	+	+	+	+
Chalouhi (2015)	+	+	X	+	+	+	X

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DEFINITE	Meta-analysis result OR (95% CI)
Genital tract trauma	1.67 (1.28-2.18) perineal 2.19 (1.13-4.24) vaginal 5.70 (1.40-2.00) cervical
Placenta previa, abruption	2.74 (1.57-4.79)
Prior PPH	2.25 (1.02-4.96)
Prolonged labor	1.76 (1.53-2.03)
Asian race	1.39 (1.33-1.46)
Diabetes	1.22 (1.08-1.39)

LIKELY	Meta-analysis result OR (95% CI)
Uterine rupture	2.35 (1.65-3.35)
Multiple gestation	2.16 (1.53-3.06)
Chorioamnionitis	1.93 (1.56-2.39)
Hypertension	1.84 (1.45-2.33)
Instrumented vaginal delivery	1.67 (1.40-2.00)
Induction of labor	1.23 (1.10-1.39)
Hispanic ethnicity	1.23 (1.20-1.25)
Predelivery oxytocin exposure	1.15 (0.95-1.40)
Nulliparity	n/a

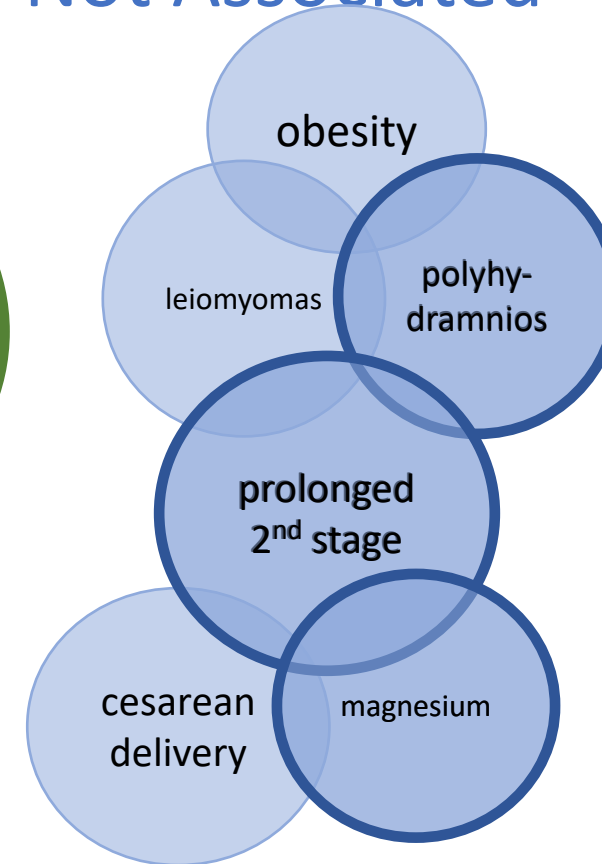
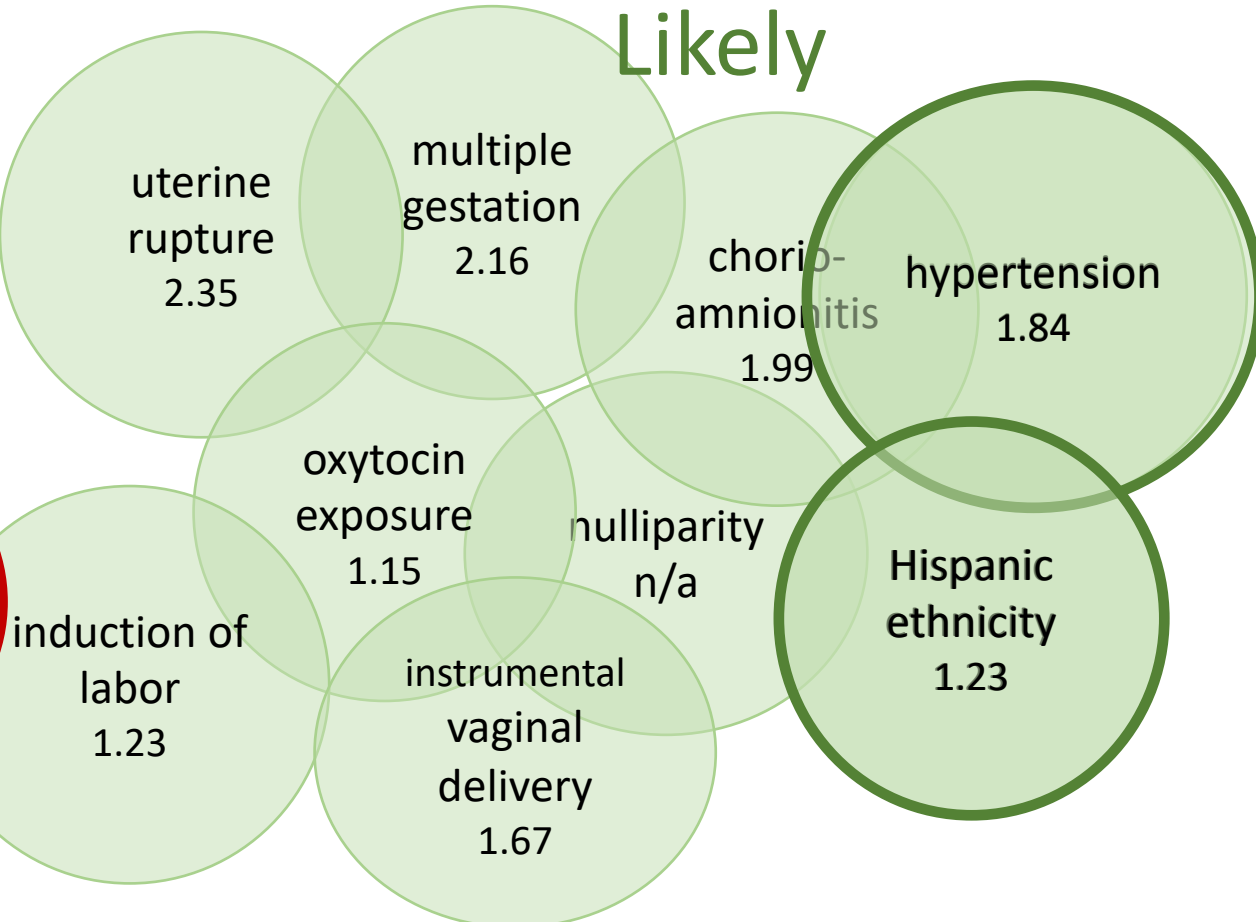
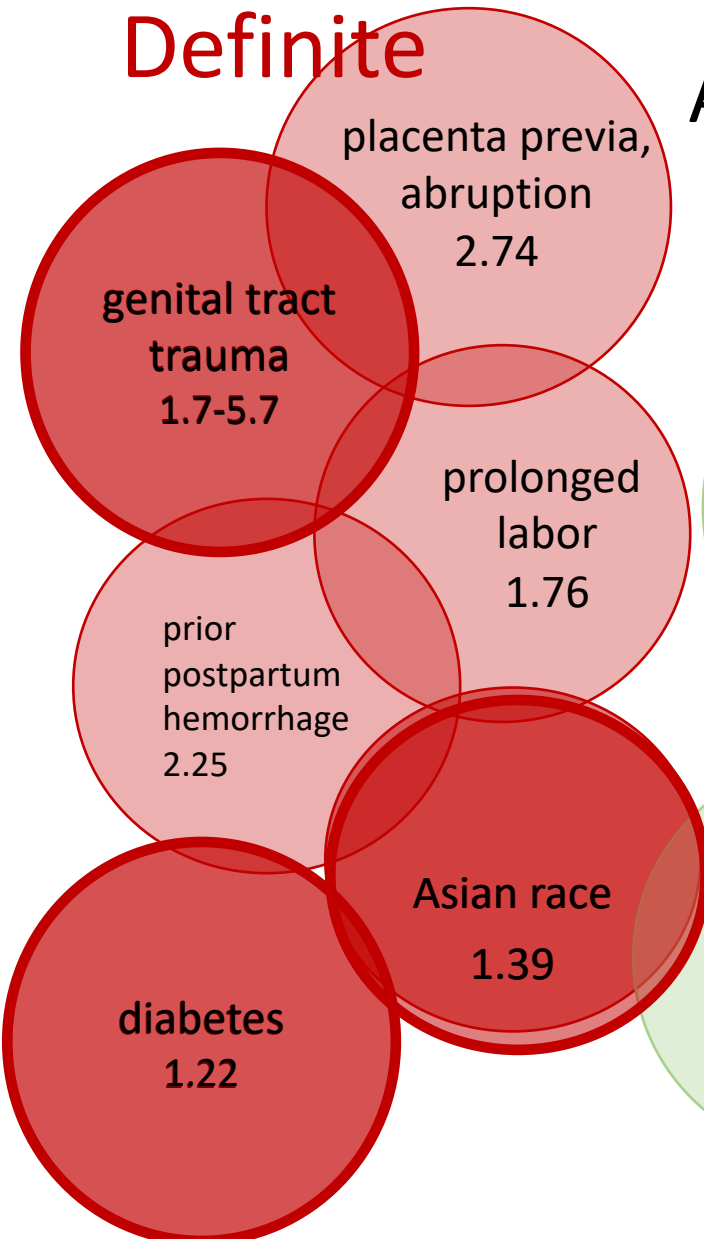
NOT ASSOCIATED
Obesity
Leiomyomas
Polyhydramnios
Magnesium
Cesarean delivery

Definite

ATONIC HEMORRHAGE RISK FACTORS

Not Associated

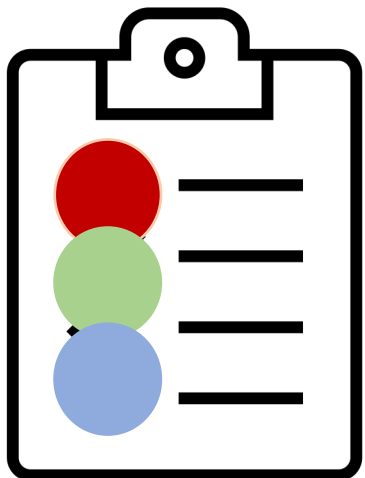
Likely



Current Commentary

Current State and Future Direction of Postpartum Hemorrhage Risk Assessment

Holly B. Ende, MD, and Alexander J. Butwick, FRCA, MS



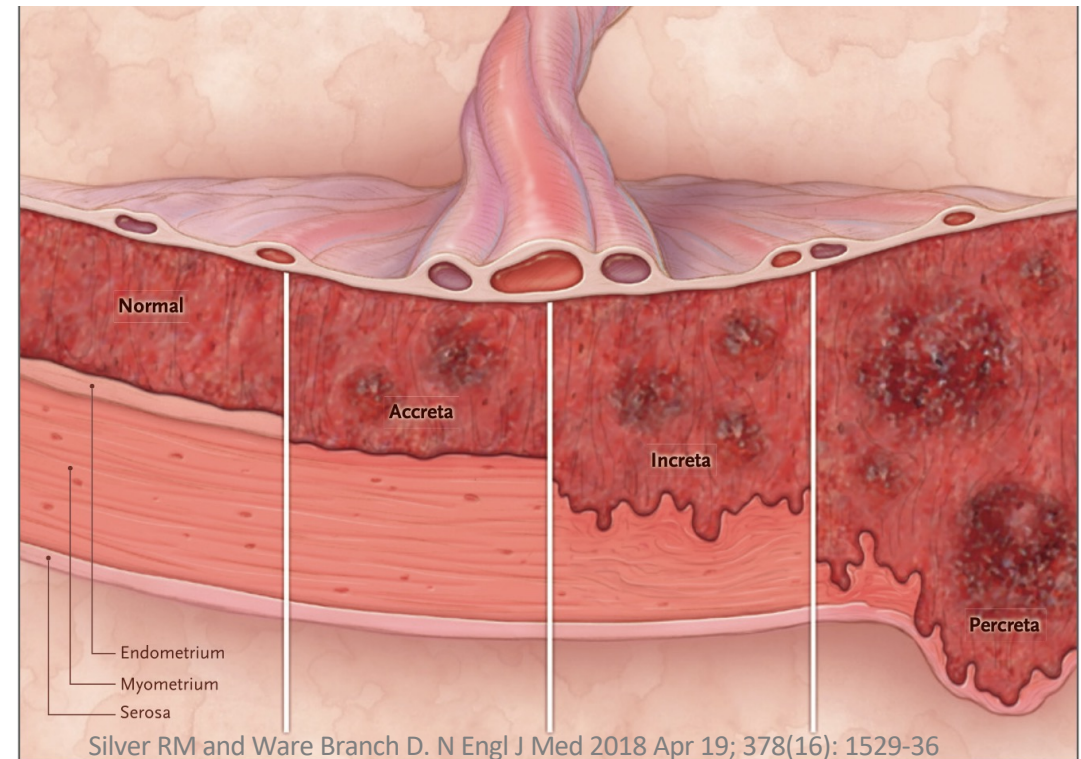
Existing Risk Assessment Tools: CMQCC, ACOG SMI, AWHONN

The Future: predictive models, machine learning, population-based studies

Maternal Morbidity Associated With Multiple Repeat Cesarean Deliveries

- 30,132 women, cesarean delivery
- 732 women: placenta previa

Prior Cesarean Deliveries	Risk of Placenta Accreta
0	3 %
1	11 %
2	40 %
3	61 %
4 or >	67 %



Incidence and risk factors for severe postpartum haemorrhage in women with anterior low-lying or praevia placenta and prior caesarean: Prospective population-based study

176 maternity units in France

Inclusion Criteria

- Placenta previa or anterior low-lying placenta
- Prior cesarean delivery
- No suspicion for placenta accreta syndrome

Primary Outcome

Severe PPH

- Blood loss \geq 1500 mL
- Transfusion \geq 4 PRBCs
- Embolization or surgical management



Incidence and risk factors for severe postpartum haemorrhage in women with anterior low-lying or praevia placenta and prior caesarean: Prospective population-based study

Inclusion Criteria

- Placenta previa or anterior low-lying placenta
- Prior cesarean delivery
- No suspicion for placenta accreta syndrome

Results: 520, 114 deliveries

- N = 230 met inclusion criteria
- **Severe PPH**: 24.8% (95% CI 19.2-30.4)
 - Placenta previa: 27.5%
 - Low-lying placenta: 15.4%
 - Unsuspected PAS: 9.9%
 - Placenta previa aOR 3.65 (95% CI 1.2-15.8)



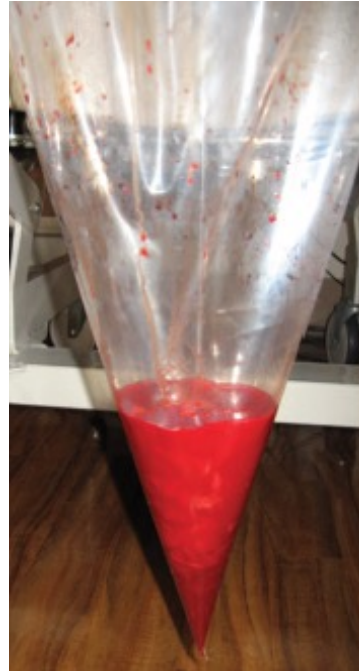
Take-home: Severe PPH was frequent, even after excluding women with PAS. Severe PPH was 2x as likely with placenta previa than with low-lying placenta.

7. Measurement of cumulative blood loss (formal, as quantitative as possible)

- What's your system?
- Calibrated drapes
- Suction canisters
- Gravimetric
- New technology?



Visual Estimation of Blood Loss After Delivery



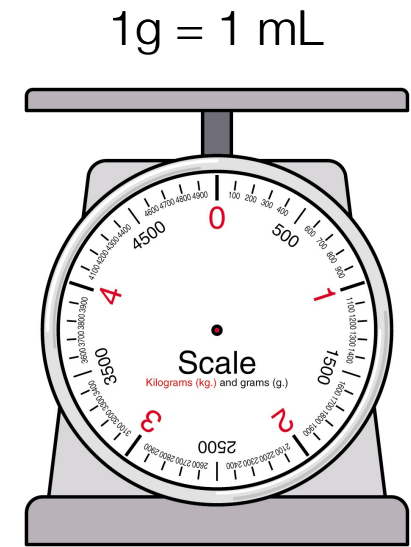
We are **REALLY BAD** at this!



Calibrated V-Drapes



Calibrated Canisters



Gravimetry



Refined Gravimetry



Colorimetry- Sponges



Colorimetry - Canisters

Introduction of a Novel System for Quantitating Blood Loss After Vaginal Delivery: A Retrospective Interrupted Time Series Analysis With Concurrent Control Group

Mario I. Lumbreras-Marquez, MBBS, MMSc,*† Sharon C. Reale, MD,†
Daniela A. Carusi, MD, MS,* Julian N. Robinson, MD,* Nora Scharf, RN, MS,‡
Kara G. Fields, MS,† and Michaela K. Farber, MD, MS†



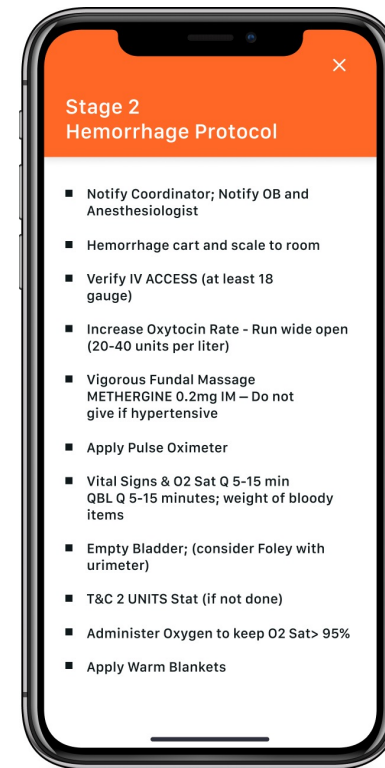
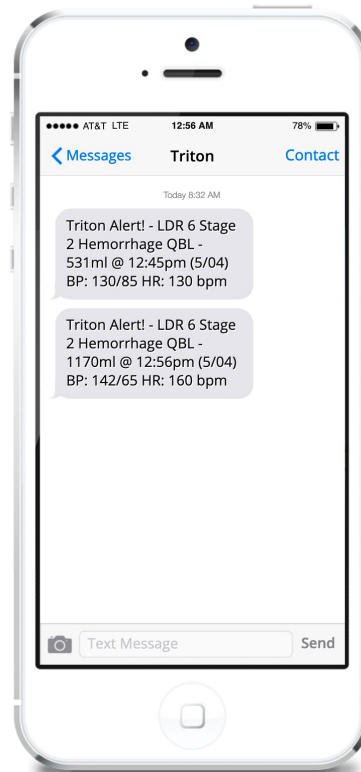
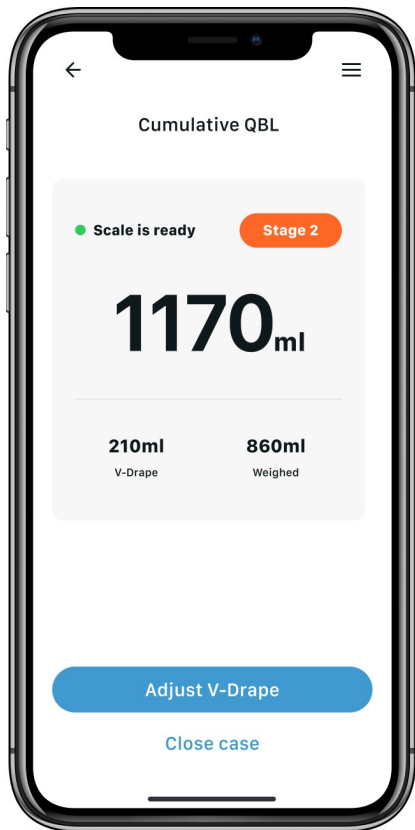
- 3 months before (vEBL)
- 3 months after (QBL)
- Primary outcome:
- Incidence of PPH detection (blood loss ≥ 500 mL)
- PPH detection before vs. after device implementation:

11.5 → 26.8%

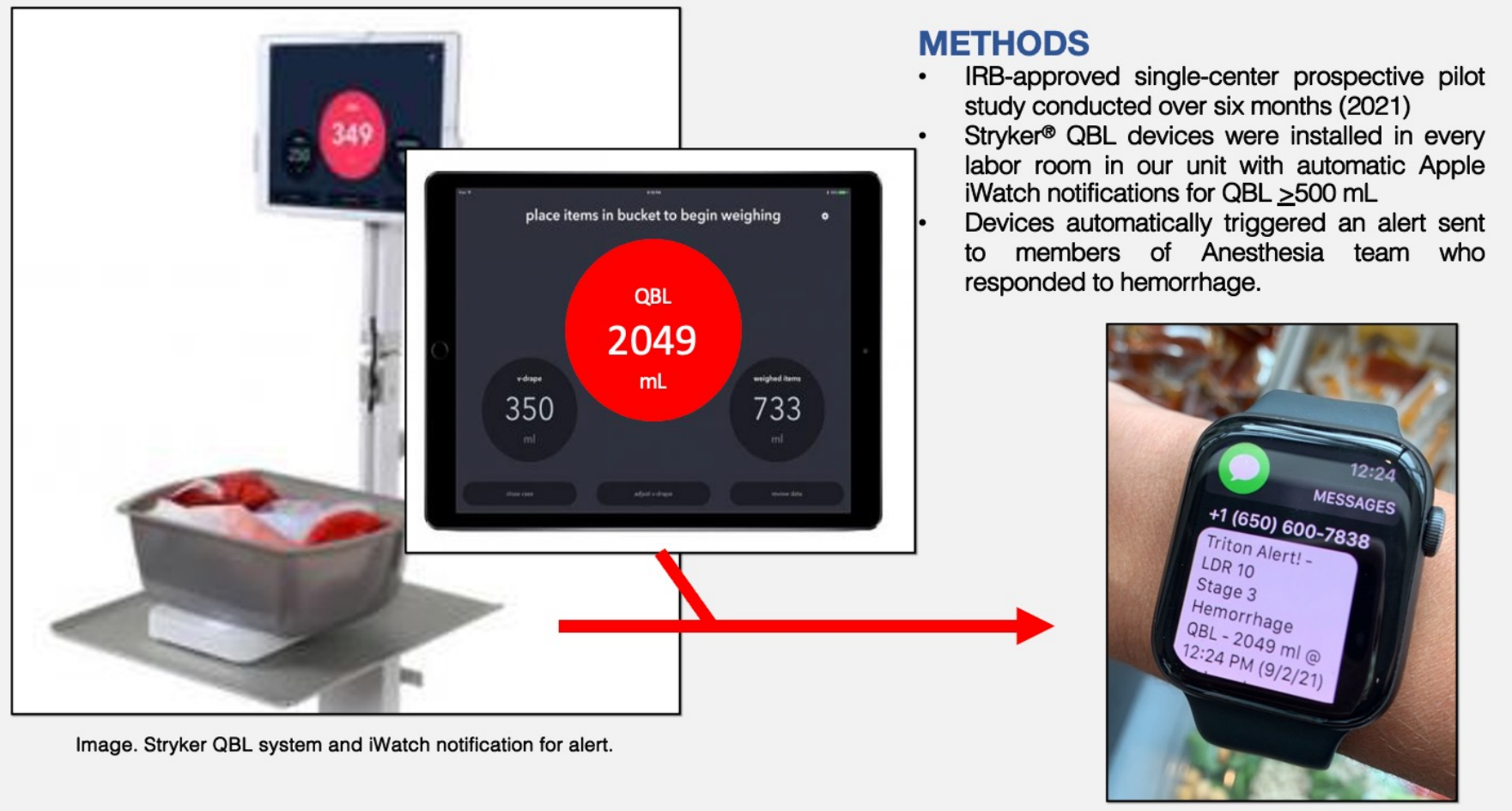
Clinician Alerts and Protocol Prompts for Active Bleeding

- Triggered by QBL ≥ 500 mL
- Vital sign thresholds input by nurse
- Staged protocol prompts provided

Triton Alert! – LDR 6 Stage 2 Hemorrhage QBL – 1263 ml @ 4:56am (10/23) BP: 99/58 HR: 138 bpm

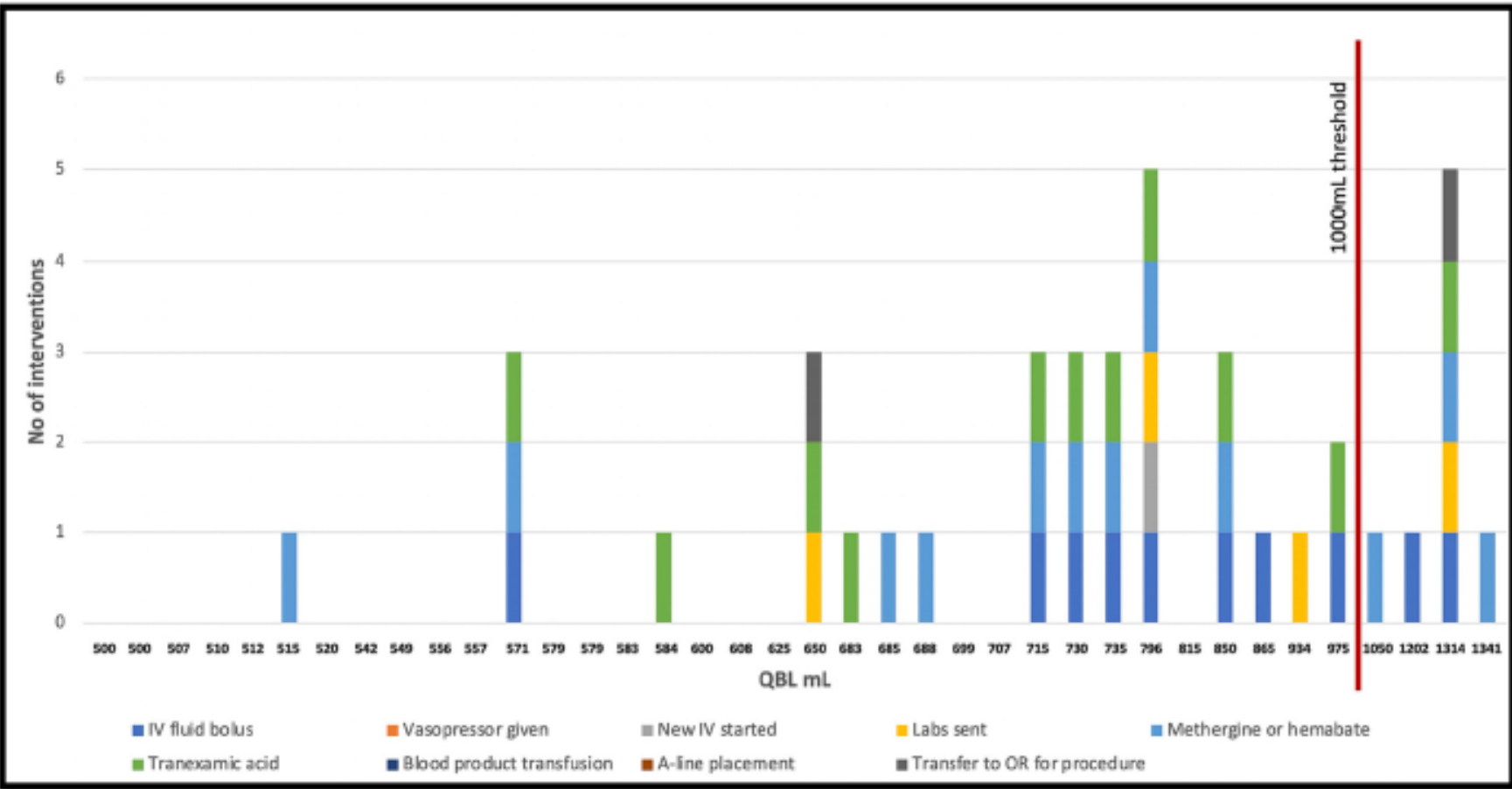


An automated clinician alert for postpartum hemorrhage after vaginal delivery



METHODS

- IRB-approved single-center prospective pilot study conducted over six months (2021)
- Stryker® QBL devices were installed in every labor room in our unit with automatic Apple iWatch notifications for $QBL \geq 500$ mL
- Devices automatically triggered an alert sent to members of Anesthesia team who responded to hemorrhage.



RESULTS

- 38 alerts, convenience sample
- Median alert QBL: 637 mL
- 50% of alerts: intervention
- 90%: occurred < 1000 mL

Most common interventions:

- Second uterotonic (31%)
- Tranexamic acid (28%)
- IV fluid bolus (23%)

Correlation coefficient between QBL and # interventions: 0.63 (P < 0.001)

Key point: a QBL threshold of 500 mL is a clinically important trigger for intervention for hemorrhage after vaginal delivery

Objectives: Postpartum Hemorrhage

- **Optimize** your unit policies overall, with focus on risk assessment and early detection
- **Recognize** the latest evidence for pharmacologic treatment modalities
- **Integrate** an up-to-date, impactful obstetric hemorrhage protocol



Objectives: Postpartum Hemorrhage

- Latest Evidence for Pharmacologic

Treatment Modalities:

Tranexamic Acid

Calcium

Methylergonovine



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1. Hemorrhage cart with supplies, checklist, and instruction cards for intrauterine balloons and compression stitches
2. Immediate access to hemorrhage medications (kit or equivalent)
3. Establish a response team (blood bank, advanced gynecology, obstetrics, and tertiary services)
4. Establish massive and emergency-release transfusion protocols (type-0 negative or uncrossmatched)
5. Unit education on protocols, unit-based drills (with postdrill debriefs)

Recognition and Prevention (Every Patient)

6. Assessment of hemorrhage risk (prenatal, on admission, and at other appropriate times)
7. Measurement of cumulative blood loss (formal, as quantitative as possible)
8. Active management of the 3rd stage of labor (department-wide protocol)

Response (Every Hemorrhage)

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10. Support program for patients, families, and staff for all significant hemorrhages

Reporting and Systems Learning (Every Unit)

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<http://www.safehealthcareforeverywoman.org>

2. Immediate access to hemorrhage medications (kit or equivalent)

Tranexamic Acid
Calcium
Methylergonovine

Guidelines: TXA for postpartum hemorrhage

October 2017



Updated WHO Recommendation on Tranexamic Acid for the Treatment of Postpartum Haemorrhage
Highlights and Key Messages from the World Health Organization's 2017 Global Recommendation

October 2017

www.mcsprogram.org



- use TXA in *all cases of PPH*, regardless of the bleeding source or cause
- use TXA *within 3h of birth* and as soon as possible after onset of PPH.



should be considered when initial medical therapy fails

Earlier use is likely to be superior to delayed treatment

Data are insufficient to recommend it for *prophylaxis* outside of the context of research

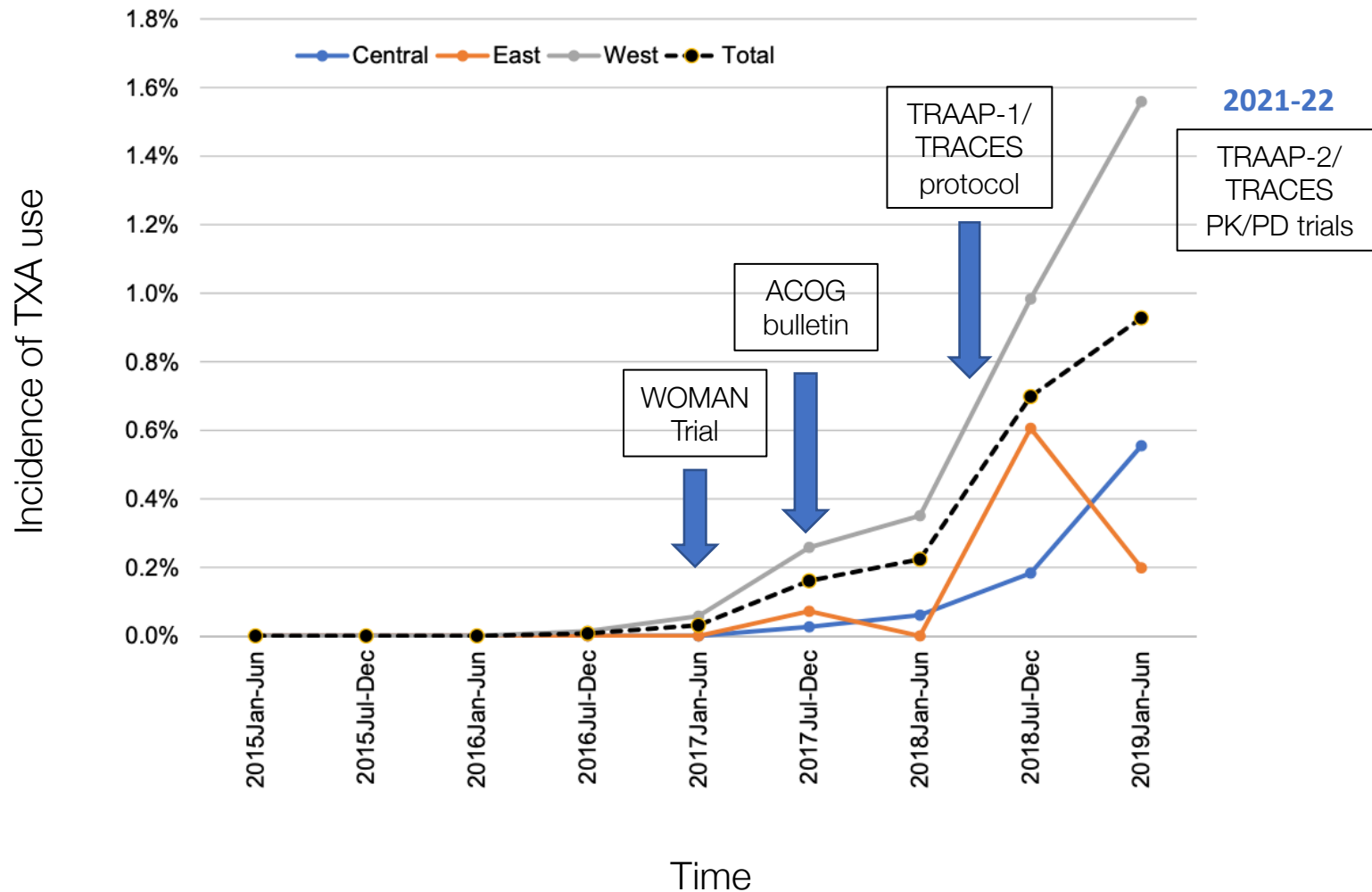


June 2021

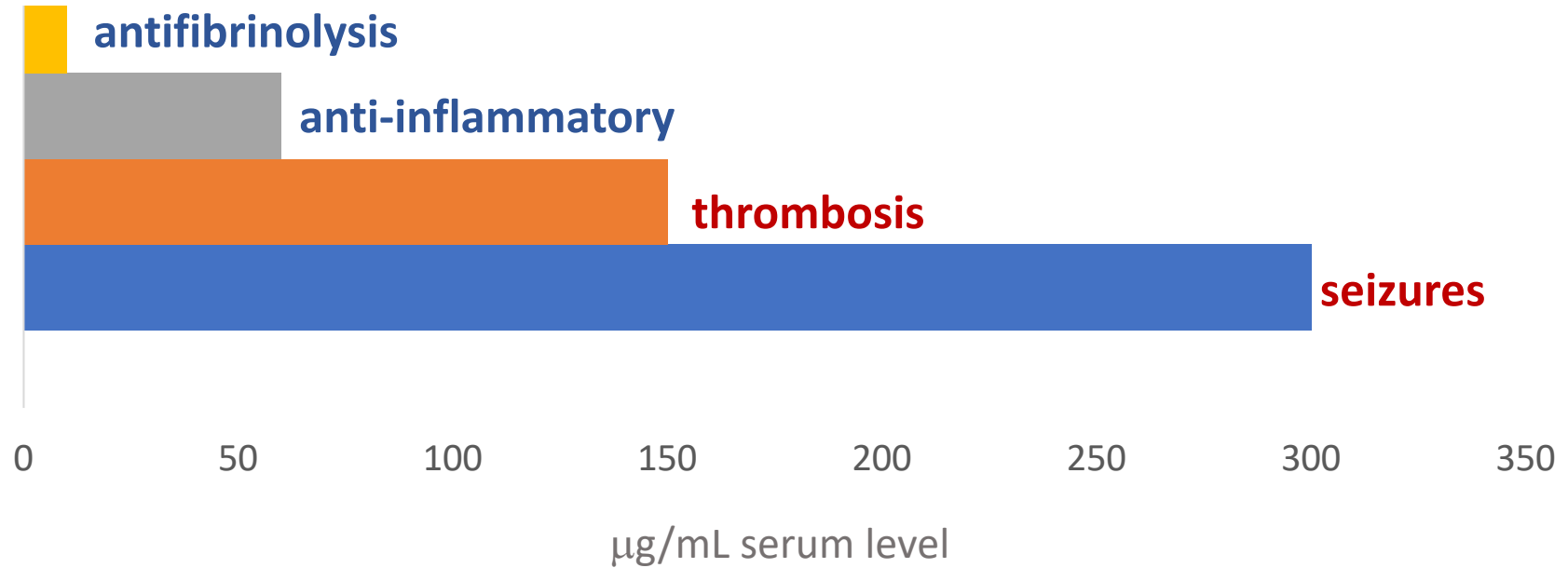


- Early use *within 3h* of clinical diagnosis
- Always *in addition to* standard care

National trends of peripartum tranexamic acid use by region in the United States, 2015-2019



Tranexamic Acid Plasma Level: Efficacy vs. Toxicity

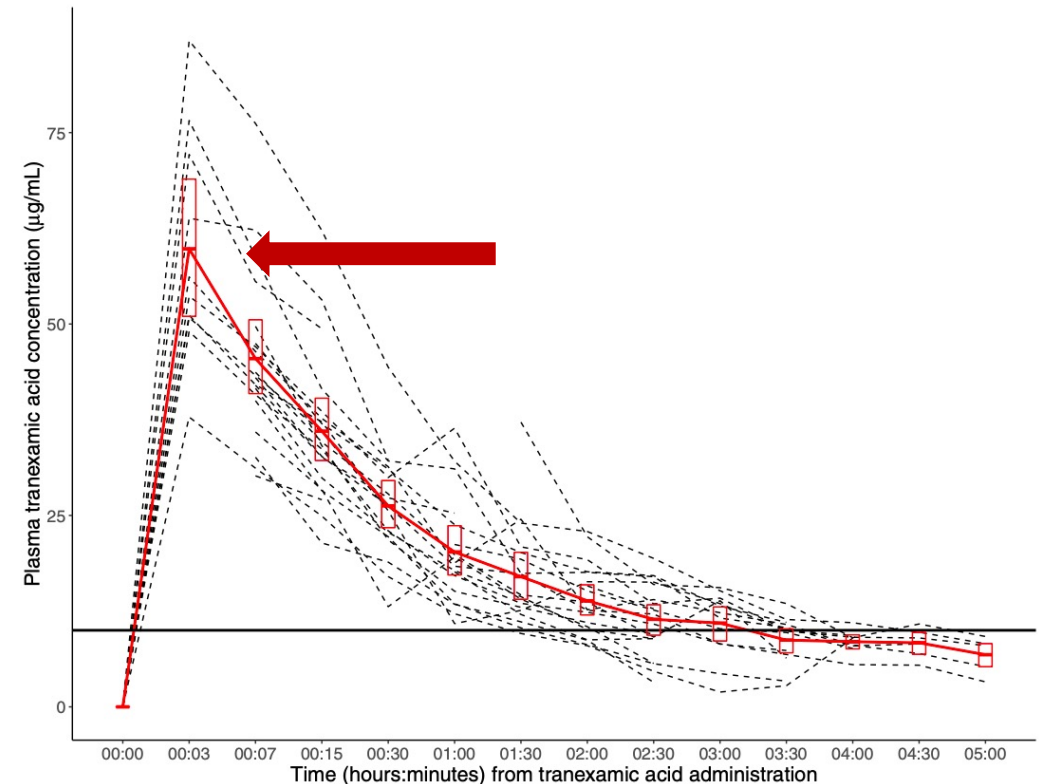


What **serum level of TXA** do we actually achieve with **1g IV given during postpartum hemorrhage**?

- A mean **peak of 60 $\mu\text{g/mL}$**
3 minutes after dosing
- Serum levels **above 10 $\mu\text{g/mL}$**
for an hour after dosing



FIGURE 1
Tranexamic acid plasma concentrations



Values are presented as mean (standard error). The *black line* highlights the 10 $\mu\text{g/mL}$ threshold.

Seifert. Tranexamic acid: maternal pharmacokinetics and pharmacodynamics. *Am J Obstet Gynecol* 2022.

Tranexamic acid for the prevention of postpartum hemorrhage in women undergoing cesarean delivery: an updated meta-analysis

Ioannis Bellos, MD; Vasilios Pergialiotis, MD, PhD



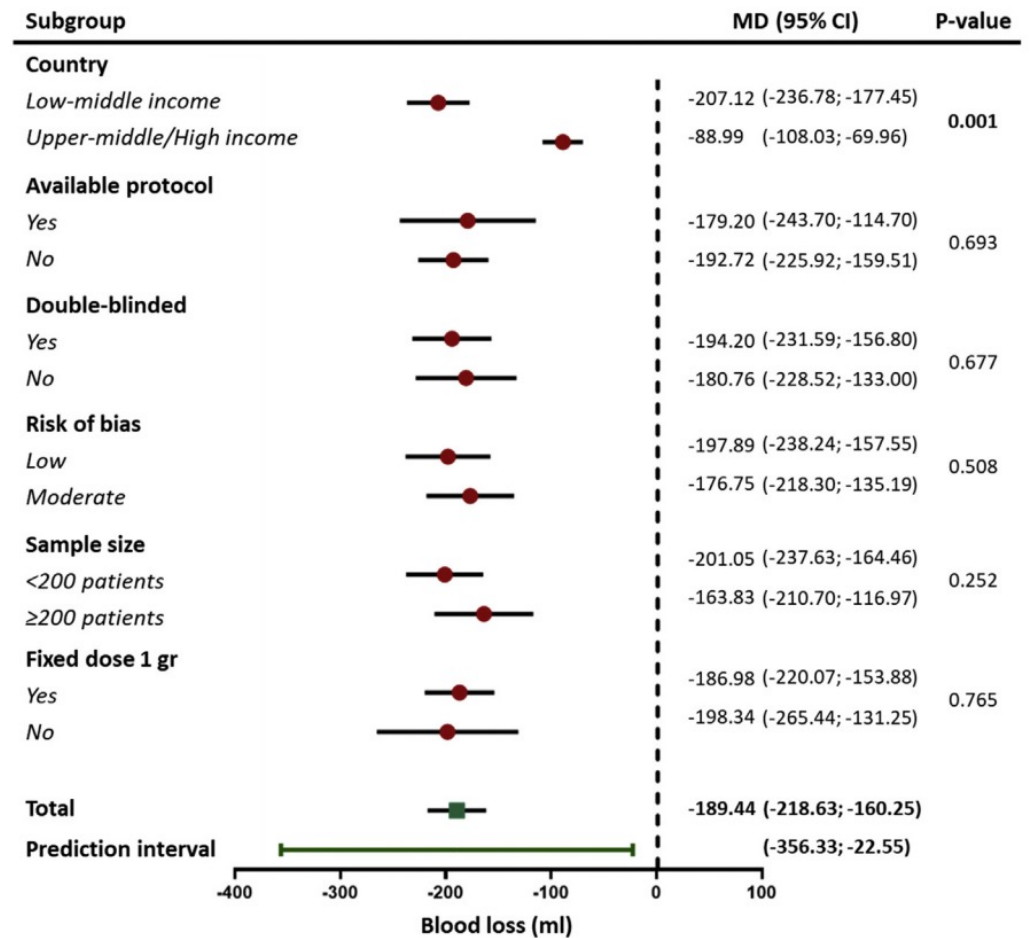
- 36 randomized controlled trials
- n = 10,659
- 1g in most trials
- 7 trials used a 10mg/kg dose

Conclusion:

Prophylactic TXA is effective in limiting PPH

- Especially in low-middle income countries

FIGURE 2
Subgroup analysis of the total blood loss outcome



CI, confidence intervals; MD, mean difference.

Bellos. Prophylactic tranexamic acid in cesarean delivery. *Am J Obstet Gynecol* 2022.

Tranexamic acid for the prevention of postpartum hemorrhage in women undergoing cesarean delivery

estimated blood loss was used in the meta-analysis. Because TRAAP2 observed a statistically significant reduction in estimated blood loss but not gravimetric blood loss, this raises the possibility of selective reporting bias in favor of TXA affecting the results of the meta-analysis.

Loïc Sentilhes, MD, PhD
Department of Obstetrics and Gynecology
Bordeaux University Hospital
Place Amélie Raba Léon

The results of the TRAAP2 trial also stand out. Unlike the other, poorer quality trials, TRAAP2 did not observe any evidence for a beneficial effect of TXA on gravimetrically measured blood loss or other related outcomes such as blood transfusion. Yet, in this meta-analysis, the reliable evidence generated by the TRAAP2 trial has been distorted by the numerous substandard clinical trials that pervade this important research topic. TRAAP2 is the only trial completed to date that reliably assesses the effects of TXA for preventing PPH. The evidence from all other trials is unreliable, as are the results of meta-analyses they contribute data to.^{2,4} ■

Tranexamic Acid to Prevent Obstetrical Hemorrhage after Cesarean Delivery

Prophylaxis with Tranexamic Acid: **Is it warranted?**

- 31 US hospitals; randomized controlled trial
- 11,000 women having elective or non-elective cesarean delivery
- Cord clamping → placebo vs. TXA: 1g diluted in 40 mL normal saline
- Primary outcome: composite of maternal death or blood transfusion within 7d or by hospital discharge
- Secondary outcomes: EBL >1L, interventions, hemoglobin change



Tranexamic Acid to Prevent Obstetrical Hemorrhage after Cesarean Delivery

Table 2. Primary and Secondary Outcomes.*

Outcome	Tranexamic Acid (N=5525)	Placebo (N=5470)	Relative Risk or Mean Difference (95% CI) [†]
Primary outcome: maternal death or blood transfusion by hospital discharge or 7 days post partum, whichever was earlier — no. (%)	201 (3.6)	233 (4.3)	0.89 (0.74 to 1.07) [‡]
Maternal death	0	1 (<0.1)	—
Blood transfusion	201 (3.6)	232 (4.2)	0.86 (0.71 to 1.03)
Estimated blood loss >1 liter — no./total no. (%)	339/4641 (7.3)	368/4573 (8.0)	0.91 (0.79 to 1.05)
Intervention in response to bleeding and related complications by 7 days post partum — no. (%)	892 (16.1)	986 (18.0)	0.90 (0.82 to 0.97)
Surgical or radiologic intervention by 7 days post partum — no. (%)	233 (4.2)	231 (4.2)	1.00 (0.84 to 1.19)
Uterotonic agent other than oxytocin by 48 hr post partum — no. (%)	649 (11.7)	732 (13.4)	0.88 (0.80 to 0.97)
Open-label use of tranexamic acid by 7 days post partum — no. (%)	108 (2.0)	109 (2.0)	0.98 (0.75 to 1.28)
Transfusion of any blood product by 7 days post partum — no. (%)	205 (3.7)	238 (4.4)	0.85 (0.71 to 1.02)
Change in hemoglobin level — g/dl [§]	-1.8±1.1	-1.9±1.1	-0.1 (-0.2 to -0.1)

Take-home: Prophylactic TXA during cesarean delivery **did not lead to a lower rate of death or blood transfusion**

The Largest Peril of Tranexamic Acid: Intrathecal Injection

Catastrophic drug errors involving tranexamic acid administered during spinal anaesthesia

S. Patel,¹ B. Robertson² and I. McConachie³

- Accidental intrathecal injection
 - 21 cases
 - 10 deaths (48%)
 - 7 obstetric patients
 - 6 deaths (86%)



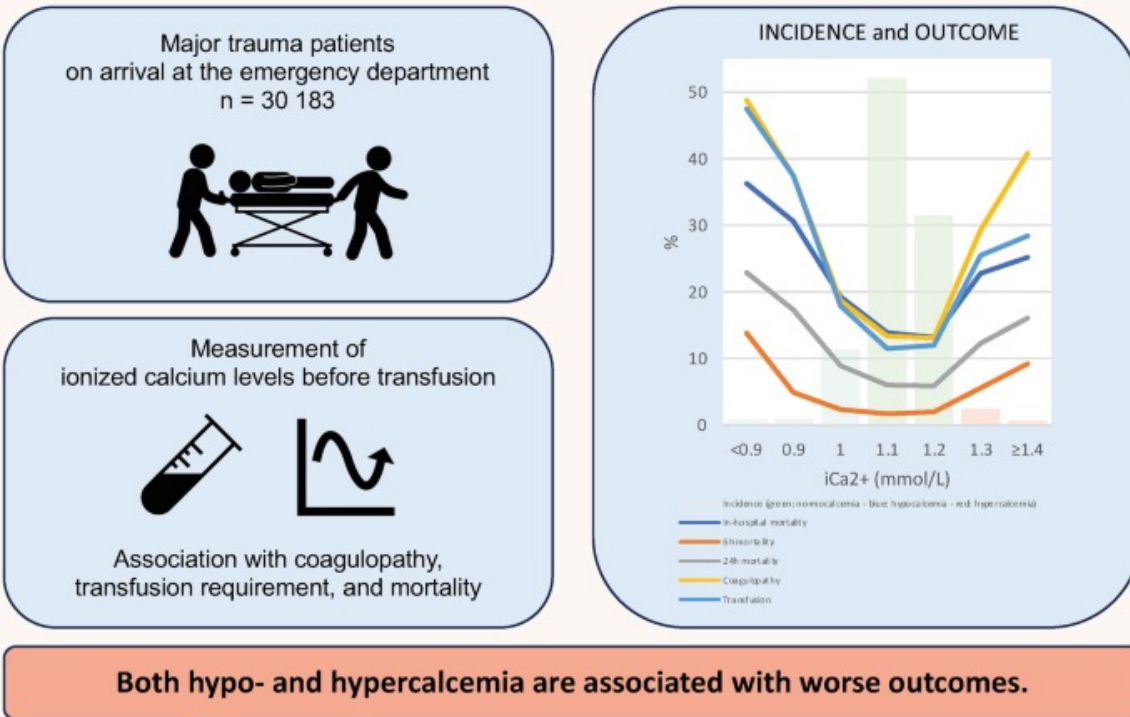
TXA for PPH:

- is not warranted for prophylaxis
- should not be prioritized over other treatments
- must be stored carefully on L&D

Calcium: Longstanding Use in Critical Care, Hemorrhage, and Transfusion

Trauma-induced disturbances in ionized calcium levels correlate parabolically with coagulopathy, transfusion, and mortality

Helsloot et al. Critical Care 2023.



- Inexpensive
- Shelf-stable
- Familiar use in obstetrics:
 - correcting transfusion-related hypocalcemia
 - treating magnesium toxicity

Uterine Effects

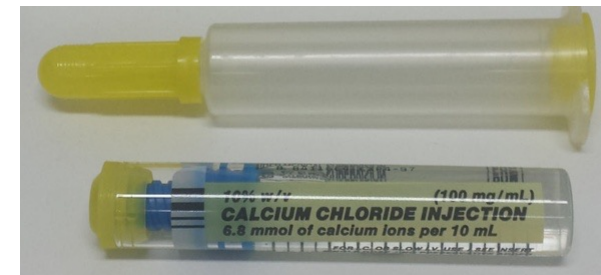
- May improve contractility
- In vitro: low calcium, lower contractility
- Laboring patients – higher calcium
- Hemorrhage risk – lower calcium

Intravenous Calcium to Decrease Blood Loss During Intrapartum Cesarean Delivery

A Randomized Controlled Trial

Hypothesis: calcium infusion will decrease blood loss at delivery in patients at risk for atonic postpartum hemorrhage

- Randomized, placebo-controlled, double-blind superiority trial
- ≥ 34 weeks, cesarean delivery after oxytocin exposure
- 1g IV CaCl₂ vs. saline, 1 min after cord clamping [both: oxytocin standard infusion]
- Primary outcome: quantitative blood loss
- Subgroup: exclusion of non-atony cases



Intravenous Calcium to Decrease Blood Loss During Intrapartum Cesarean Delivery

A Randomized Controlled Trial

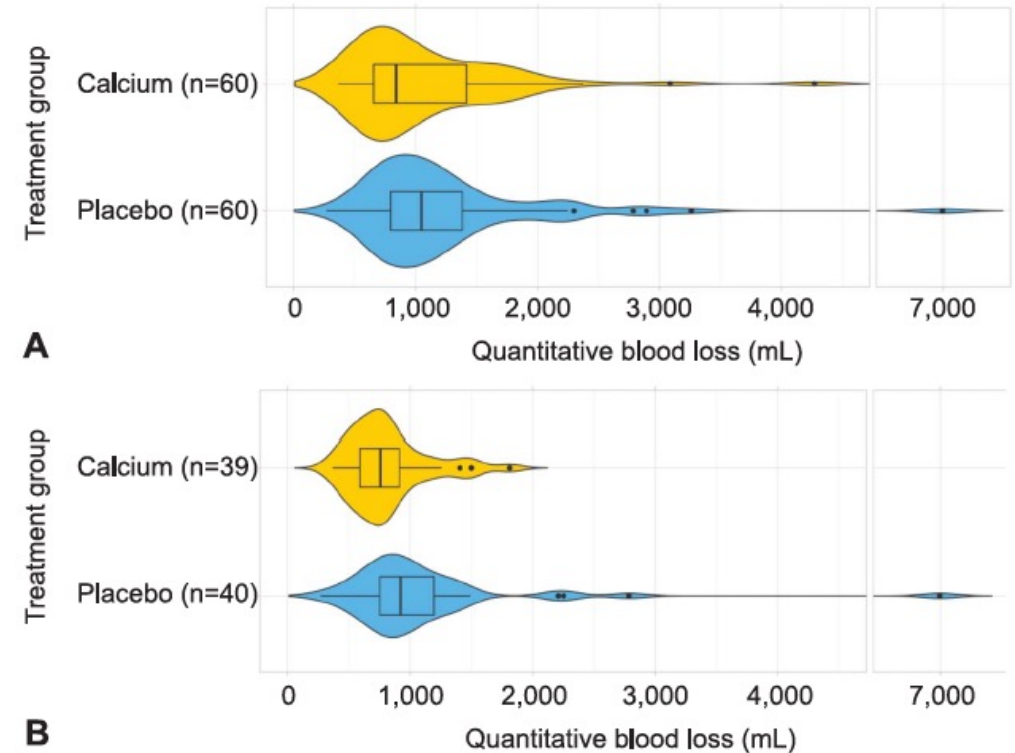
Results

828 laboring patients consented; 120 enrolled

Median QBL 840 mL (CaCl₂) vs. 1,051 mL (placebo)
QBL reduction 211 mL; NS (95% CI -33 to 410)

Subgroup n = 79 (uterine atony only)

QBL reduction 356 mL (95% CI 159-515)



Take-home: Calcium is well-tolerated, low-risk, and reasonable to consider for PPH related to uterine atony

Prophylactic Administration of Uterotonics to Prevent Postpartum Hemorrhage in Women Undergoing Cesarean Delivery for Arrest of Labor

A Randomized Controlled Trial

Mrinalini Balki, MD, Kristi Downey, MSc, Andrew Walker, PhD, Gareth Seaward, MMed, and Jose C. A. Carvalho, MD, PhD



Question: Does prophylactic secondary uterotonic prevent postpartum hemorrhage during cesarean delivery for failure to progress?

- Arrest of labor
 - ≥ 4 h on oxytocin
 - Double-blind, 3-arm RCT
 - Tone checks: 3,5,10 min
 - **Primary outcome: intraoperative need for additional uterotonics**
- Diagram showing three arms of the RCT:
- Oxytocin alone 5 IU IV
 - Oxytocin + ergonovine 0.25mg IV
 - Oxytocin + carboprost 0.25 mg IM

Box 1. Protocol for Administration of Additional Uterotonics (Open Label)

1st uterotonic

- Oxytocin 5 international units bolus over 1 min

2nd uterotonic

- Carboprost 0.25 mg intramyometrial OR Ergonovine 0.25 mg intramuscular

3rd uterotonic

- Carboprost 0.25 mg intramyometrial 15 min after the previous dose OR Ergonovine 0.25 mg intramuscular (IF not yet given)

Prophylactic Administration of Uterotonics to Prevent Postpartum Hemorrhage in Women Undergoing Cesarean Delivery for Arrest of Labor

A Randomized Controlled Trial

Mrinalini Balki, MD, Kristi Downey, MSc, Andrew Walker, PhD, Gareth Seaward, MMed, and Jose C. A. Carvalho, MD, PhD

	Oxytocin alone (n = 35)	Oxytocin plus ergonovine (n = 33)	Oxytocin plus carboprost (n = 32)	P value
Additional uterotonics	13 (37%)	11 (33%)	11 (34%)	0.932
Tone at 3 min	22 (63%)	19 (58%)	21 (66%)	0.814
EBL (mL)	676 ± 183	663 ± 143	714 ± 309	0.644
Nausea, vomiting	18 (51%)	28 (85%) OR 5.3 (1.7-16.9)	23 (72%) OR 2.4 (0.9-6.7)	0.010
Hypotension	14 (40%)	5 (15%)	8 (25%)	0.068

Take-home: for patients having CD after labor with oxytocin augmentation, there is no benefit to prophylactic ergonovine or carboprost.

Prophylactic Methylergonovine and Oxytocin Compared With Oxytocin Alone in Patients Undergoing Intrapartum Cesarean Birth

A Randomized Controlled Trial

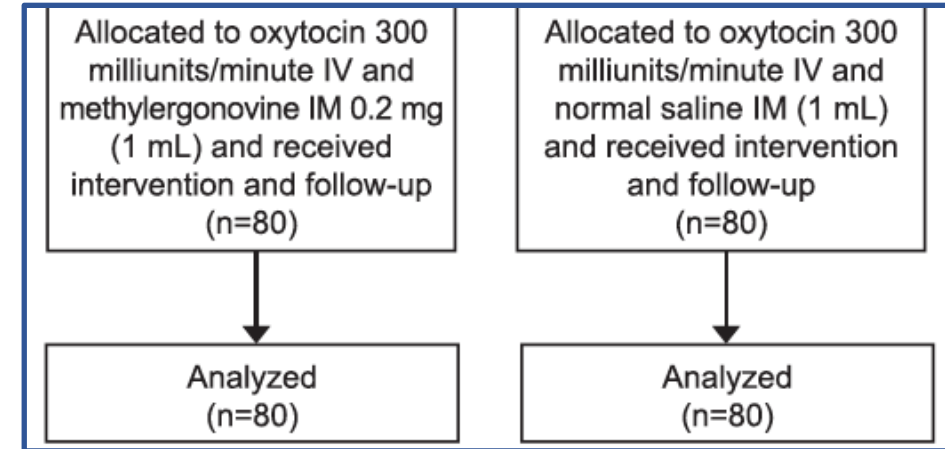
Nicole Masse, MD, Franklin Dexter, MD, PhD, and Cynthia A. Wong, MD

Single-center, randomized placebo-controlled trial
1088 approached on arrival to L&D
160 enrolled at time of failure to progress cesarean

Oxytocin plus prophylactic methylergonovine:

- lower additional uterotonic 20 vs 55%, RR 0.4, 95% CI 0.2-0.6
- more satisfactory tone 80 vs. 41% RR 1.9, 95% CI 1.5-2.6
- lower PPH 35 vs. 59% RR 0.6, 95% CI 0.4-0.9
- lower QBL 967 vs 1315 mL mean diff 348, 95% CI 124-572
- lower transfusion 5 vs 23% RR 0.2, 95% CI 0.1-0.6

N = 160 randomized



Take-home: for patients having CD after labor with oxytocin augmentation, there ~~is no~~ may be benefit to prophylactic Ergonovine!

-IM vs IV?

-different oxytocin dosing?



Objectives: Postpartum Hemorrhage

- **Optimize** your unit policies for hemorrhage risk assessment and delivery planning
- **Recognize** the latest evidence for pharmacologic treatment modalities
- **Integrate** an up-to-date, impactful obstetric hemorrhage protocol



Objectives: Postpartum Hemorrhage

- **Update your obstetric hemorrhage protocol: Coagulation Testing?**



Box 1. Obstetric Hemorrhage Safety Bundle From the National Partnership for Maternal Safety, Council on Patient Safety In Women's Health Care

Readiness (Every Unit)

1. Hemorrhage cart with supplies, checklist, and instruction cards for intrauterine balloons and compression stitches
2. Immediate access to hemorrhage medications (kit or equivalent)
3. Establish a response team—who to call when help is needed (blood bank, advanced gynecologic surgery, other support and tertiary services)
4. Establish massive and emergency-release transfusion protocols (type-0 negative or uncrossmatched)
5. Unit education on protocols, unit-based drills (with postdrill debriefs)

Recognition and Prevention (Every Patient)

6. Assessment of hemorrhage risk (prenatal, on admission, and at other appropriate times)
7. Measurement of cumulative blood loss (formal, as quantitative as possible)
8. Active management of the 3rd stage of labor (department-wide protocol)

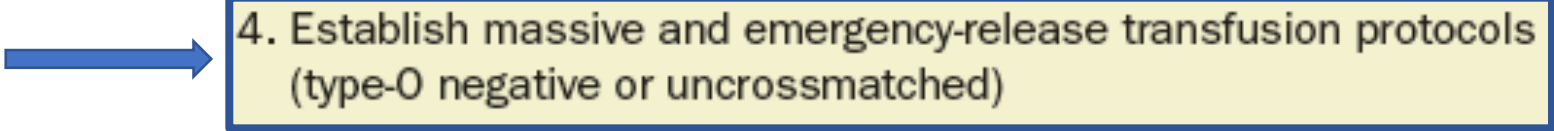
Response (Every Hemorrhage)

9. Unit-standard, stage-based obstetric hemorrhage emergency management plan with checklists
10. Support program for patients, families, and staff for all significant hemorrhages

Reporting and Systems Learning (Every Unit)

11. Establish a culture of huddles for high-risk patients and postevent debriefs to identify successes and opportunities
12. Multidisciplinary review of serious hemorrhages for systems issues
13. Monitor outcomes and process metrics in perinatal quality improvement committee

<http://www.safehealthcareforeverywoman.org>



4. Establish massive and emergency-release transfusion protocols (type-0 negative or uncrossmatched)

**detection and treatment of coagulopathy*

Morbidity from Postpartum Hemorrhage: 75% Preventable

Preventable Issues

Underestimation of blood loss

Missing signs of hypovolemic shock

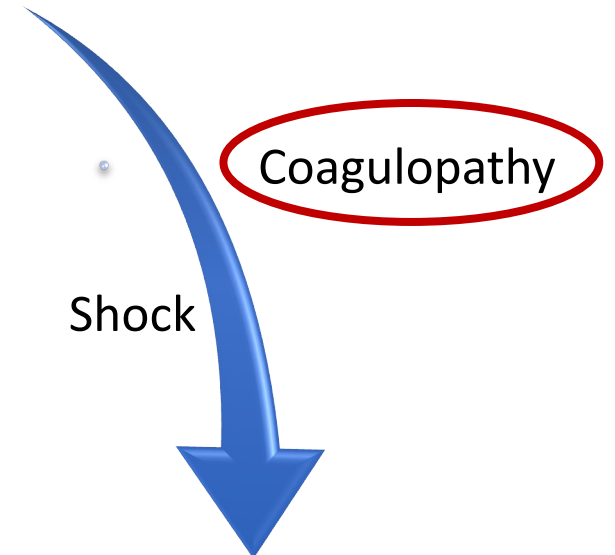
Late activation of MTP

Inadequate resuscitation

Failure to call for expert help

“Too Little Done Too Late”

Unchecked
bleeding



Shock

Cardiac arrest

EXAMPLE

Obstetric Hemorrhage Checklist

Complete all steps in prior stages plus current stage regardless of stage in which the patient presents.

RECOGNITION:

Call for assistance (Obstetric Hemorrhage Team)

Designate: Team leader _____ Checklist reader/recorder Primary RN

Announce: Cumulative blood loss Vital signs _____ Determine stage

STAGE 1: BLOOD LOSS > 500 mL vaginal OR blood loss > 1000 mL cesarean with normal vital signs and lab values

INITIAL STEPS:

- Ensure 16G or 18G IV Access
- Increase IV fluid (crystalloid without oxytocin)
- Insert indwelling urinary catheter
- Fundal massage

MEDICATIONS:

- Ensure appropriate medications given patient history
- Increase oxytocin, additional uterotonics

BLOOD BANK:

- Type and Crossmatch 2 units RBCs

ACTION:

- Determine etiology and treat
- Prepare OR, if clinically indicated (optimize visualization/examination)

Oxytocin (Pitocin):

10-40 units per 500-1000mL solution

Methylergonovine (Methergine):

0.2 milligrams IM; **Avoid with hypertension**

15-methyl PGF₂α (Hemabate, Carboprost):

250 micrograms IM (may repeat in q15 minutes, maximum 8 doses); **Avoid with asthma; use with caution with hypertension**

Misoprostol (Cytotec):

800-1000 micrograms PR
600 micrograms PO or 800 micrograms SL

Tone (i.e., atony)

Trauma (i.e., laceration)

Tissue (i.e., retained products)

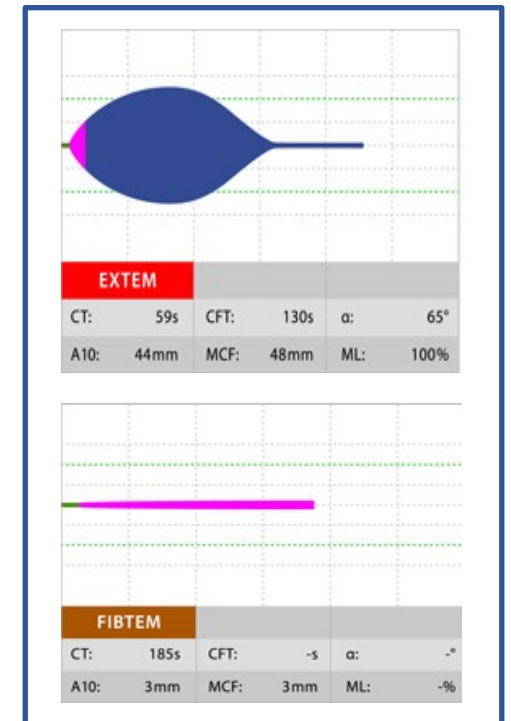
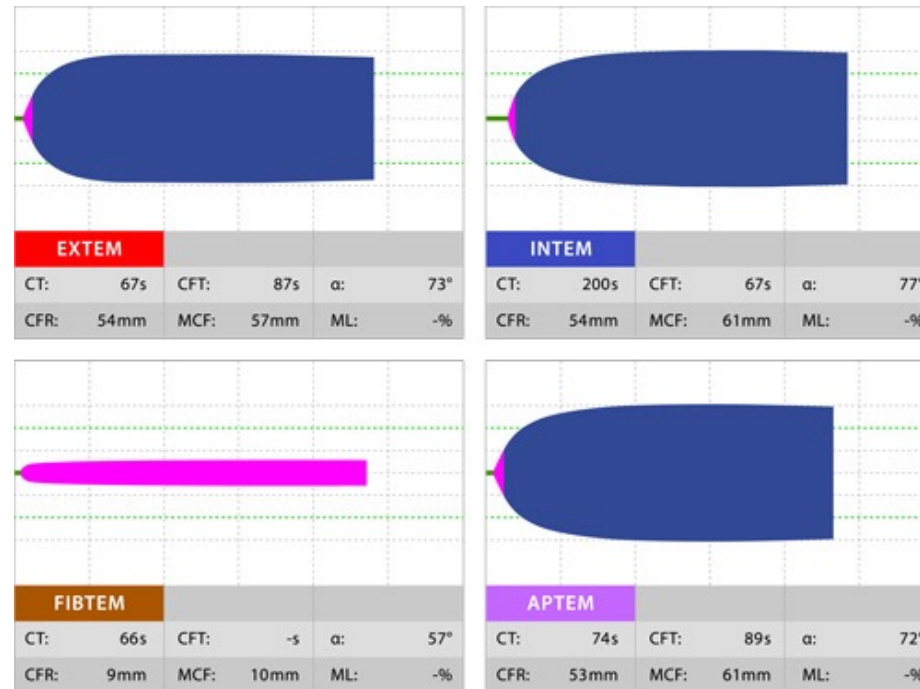
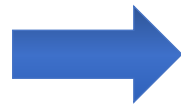
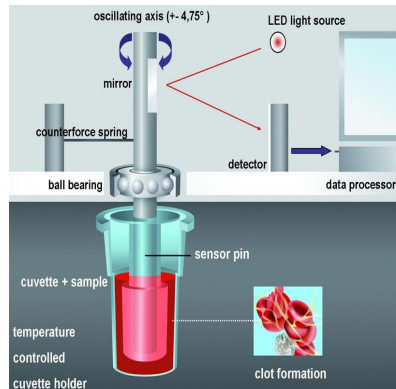
Thrombin (i.e., coagulation dysfunction)

Coagulopathy Detection During Postpartum Hemorrhage: You have Choices!



Low fibrinogen state?
FIBTEM

Hyperfibrinolysis?
APTEM



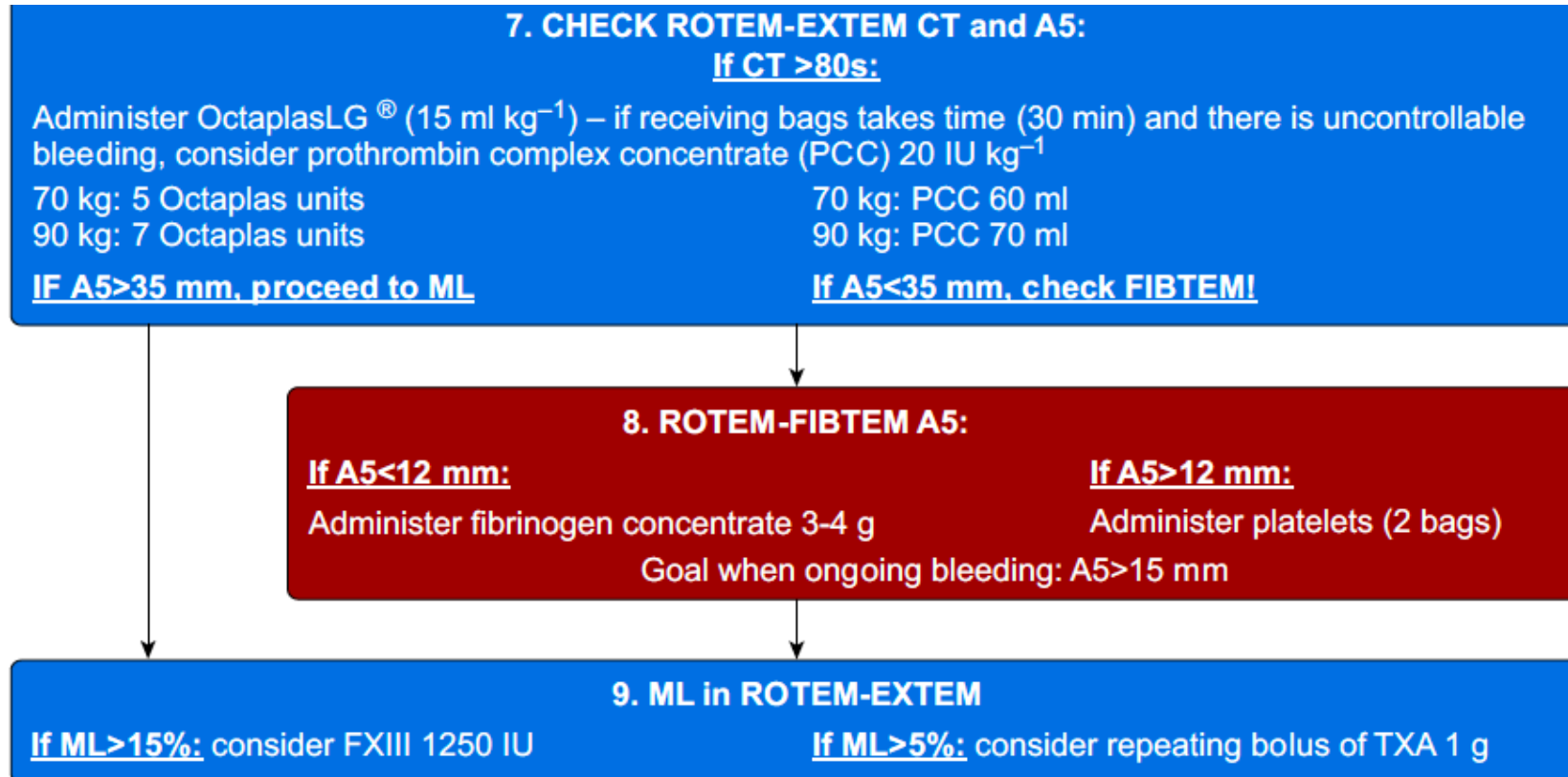
Thromboelastometry-guided treatment algorithm in postpartum haemorrhage: a randomised, controlled pilot trial

Hypothesis: a ROTEM-guided protocol will decrease the need for **red blood cell transfusion**.



- Single center, single-blinded randomized controlled trial
- January 2016- September 2019
- Severe PPH: QBL \geq 1500 mL
- Primary outcome: blood product transfusion

Thromboelastometry-guided treatment algorithm in postpartum haemorrhage: a randomised, controlled pilot trial



Results

54 patients

Products transfused, ROTEM vs. Control:

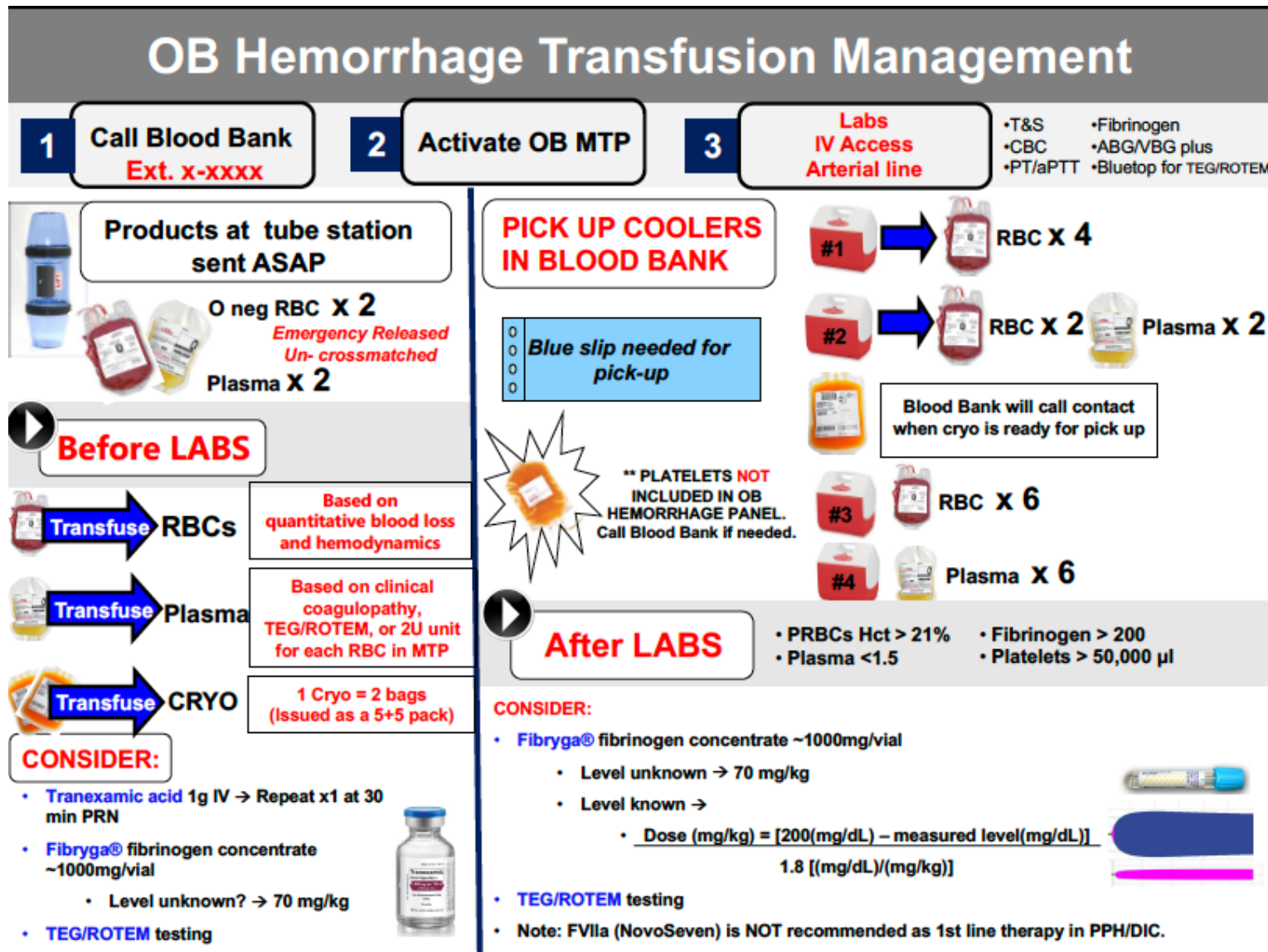
- PRBCs 2 vs 3 (P = 0.399)
- Plasma 5 vs 12 (p = 0.040)
- No other differences!

Take-home: ROTEM use during severe PPH did not lower blood transfusion but was associated with less plasma administration.

Point-of-care coagulation testing for postpartum hemorrhage: Key points

- There's **limited evidence** from randomized controlled trials to support POCCT integration into hemorrhage protocols.
- Many algorithms include them anyway.
- **Robust studies are difficult to conduct!**
 - Obstetric emergency situations preclude enrollment
 - Coagulopathy cases are very rare
 - Studies are underpowered for the outcome of transfusion
 - Patient and bleeding heterogeneity
 - Bias from lack of blinding
 - Protocol adherence can be low

An OB-Specific Massive Transfusion Protocol



After LABS

- PRBCs Hct > 21%
- Plasma < 1.5
- Fibrinogen > 200
- Platelets > 50,000 µl

CONSIDER:

- Fibryga® fibrinogen concentrate ~1000mg/vial
 - Level unknown → 70 mg/kg
 - Level known →
 - Dose (mg/kg) = $\frac{[200(\text{mg/dL}) - \text{measured level}(\text{mg/dL})]}{1.8 [(\text{mg/dL}) / (\text{mg/kg})]}$
- TEG/ROTEM testing
- Note: FVIIa (NovoSeven) is NOT recommended as 1st line therapy in PPH/DIC.



**** PLATELETS NOT INCLUDED IN OB HEMORRHAGE PANEL. Call Blood Bank if needed.**

***IMMEDIATE, ORGANIZED RELEASE OF BLOOD PRODUCTS**

***FIBRINOGEN SOURCES**
***TRANEXAMIC ACID**
***COAGULATION TESTING**

Conclusion: Postpartum Hemorrhage

- **Unit Protocols:** can always be improved!
- **Risk assessment:** standardize it to your unit, with continued refinement
- **Detection:** do quantitate blood loss
- **Tranexamic acid:** use for treatment, not for prophylaxis
- **Calcium:** consider for patients with atonic hemorrhage
- **Methergine:** prophylaxis good for hi-risk
- **Coagulopathy detection:** incorporate it in your hemorrhage protocol



Thank you!

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