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Massive Hemorrhage Protocol (MHP) How do I do it?

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Disclosures

- Advisory board participation: Alexion, Shire/Takeda, Ablynx/Sanofi
- Honoraria for speaking: Alexion, Sanofi, Shire/Takeda
- Clinical trials: Ablynx/Sanofi, Bioverativ/Sanofi

- None are relevant to the content of this talk

Learning Objectives

- Provide definition of massive hemorrhage
- Define massive transfusion protocol and its benefits
- Describe the elements of an optimal hospital MHP for adult patients

What is a Massive Hemorrhage?

- No widely accepted universal definition:
  - 10 units in 24 hrs, 6 RBC in 4 hours, etc.
  - Amount and rate of bleeding as well as likelihood of being able to rapidly achieve hemostasis
- Rare, complex and high stress medical scenario
- Associated with a high mortality rate

What is a Massive Hemorrhage?

- Massive hemorrhage may occur in the context of:
  - Trauma
  - Post-partum
  - Cardiovascular event (ex. ruptured abdominal aortic aneurysm, iatrogenic vessel injury, etc.)
  - Acute upper GI bleeding

What is a Massive Hemorrhage Protocol (MHP)?

- Protocol, systematic clinical workflow, algorithm, integrated care pathway
  - Aim (7 **R**'s):
    - **R**ight health care workers, doing the **r**ight things, for **r**ight patients, in the **r**ight order, at the **r**ight time, in the **r**ight place, with the **r**ight outcome
  - Outcomes:
    - Leads to improved outcomes

Gawande 2009; Haynes et al NEJM 2009 ; Allen et al JBI Libr Syst Rev 2009

Are There Proven Benefits of MHP?

- MHP implementation is associated with
  - Reduction in mortality, organ failure, post-injury complications
    - independent of what exactly is in the protocol
  - Faster delivery of blood components to patient
  - Not associated with increase in blood component wastage
  - Less blood component utilization (and less cost)
  - Decreased length of hospital stay

Dente et al J Trauma 2009; Cotton et al J Trauma 2009; Riskin et al J Am Coll Surg 2009; Reed et al Injury 2017; Cotton et al J Trauma 2008; O'Keeffe et al Arch Surg 2008; Khan et al Injury 2013

Effectiveness of MHPs on mortality in trauma: a systematic review and meta-analysis

Table 3 Mortality meta-analysis (random-effects model)

Study	OR (95% CI)	Weight (%)
Riskin *et al.*[18]	0.29 (0.10–0.80)	9.46
Cotton *et al.*[12]	0.32 (0.19–0.52)	16.99
O'Keeffe *et al.*[19]	1.10 (0.56–2.14)	14.22
Shaz *et al.*[16]	1.10 (0.63–1.89)	16.24
Simmons *et al.*[20]	0.75 (0.53–1.05)	19.55
Dirks *et al.*[21]	1.21 (0.41–3.61)	8.87
Sisak *et al.*[22]	1.30 (0.46–3.68)	9.35
Sinha *et al.*[23]	0.77 (0.16–3.75)	5.31
Pooled OR	0.73 (0.48–1.11)	—

CI, confidence interval; OR, odds ratio.

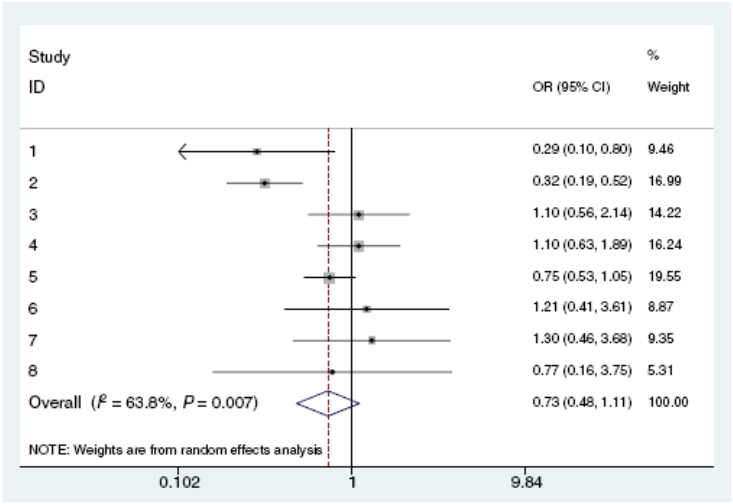


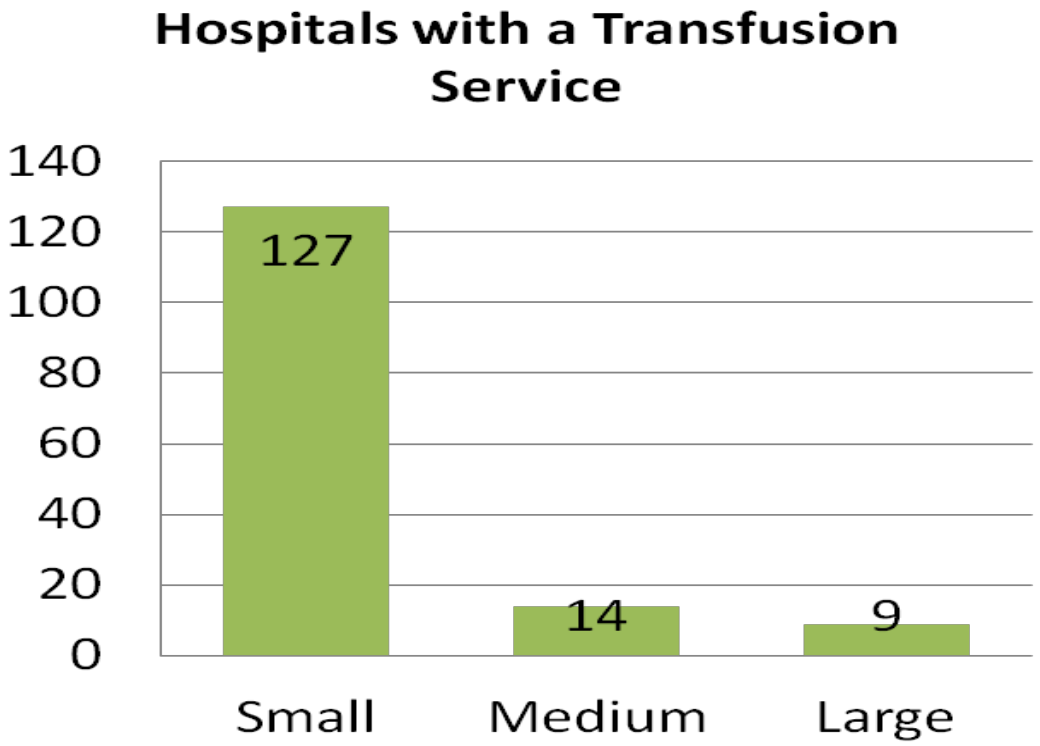
Fig. 2. Meta-analysis of mortality. CI, confidence interval; OR, odds ratio.

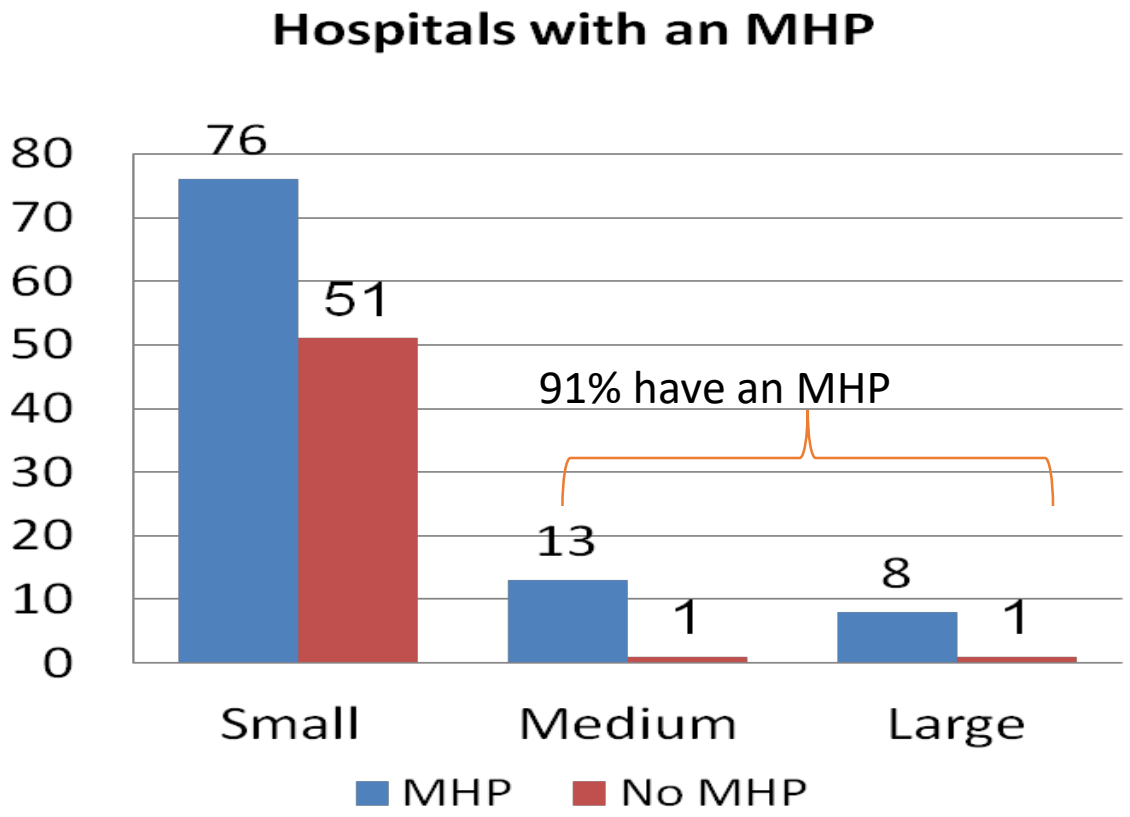
Authors' Conclusions:

- Despite the popularity of MTPs and directives mandating their use in trauma centres, in before–after studies, **MTPs have not always been associated with improved mortality**
- **Evidence-based standardization of MTPs, improved compliance** and analysis of broader endpoints were identified as areas for further research

Mitra B et al. ANZ J Surg. 2013

Ontario Survey: Hospitals with MHP (n=150)





Units of RBCs transfused in 2017
Small <5000
Medium 5000-10,000
Large > 10,000

Chin et al Injury 2019

Basic Elements of the MHP: MHP = T^7

	T
1	Triggering and Treatment of Bleeding
2	Team (incl. Training and Communication)
3	Tranexamic acid
4	Temperature
5	Testing
6	Transfusion
7	Termination and Tracking Performance

Triggering

- The protocol should be referred to as the Massive Hemorrhage Protocol (MHP) in all hospitals
- MHP is a code
  - Announced overhead as CODE TRANSFUSION
    - Announcing overhead instantaneously alerts all of the relevant parties and make bring additional resources
  - Activated by a single call to Locating/Switchboard with dissemination to all team members

Triggering

- Triggering criteria
  - May differ from hospital to hospital – KNOW YOURS
  - May be different for different patient populations
  - Volume of blood loss, number of RBC transfused, ABC score, Shock Index, traumatic bleeding severity score

Patient group	Validated activation criteria	Description
Adult	Shock Index	HR/SBP > 0.9 has 1.6x risk of massive hemorrhage
	ABC Score for trauma	1 point for: penetrating injury, BP≤90mmHg, HR≥120bpm, positive FAST Score ≥2 has higher risk of massive hemorrhage
	Resuscitation intensity	≥4 units of fluid within first 30 minutes 1 unit = 1 unit RBC or 1 unit plasma or 1L crystalloid or 500ml colloid

Treatment of Bleeding

- Damage control resuscitation
  - Immediate hemorrhage control
    - Pressure, damage control surgery, angiography, etc.
  - Restoration of blood volume and physiologic/hematologic stability
    - IV fluids
      - Early transfusion
      - Avoid too much crystalloid
    - Correct hypothermia
    - Correct acidosis
    - Correct calcium

Ball CJS 2014

Expert Support for MHP

- Any patient on whom MHP was activated and who cannot receive definitive management locally, must be considered for transfer ASAP

- CritiCall 1 800 668 4357

Team

BIG Hospital

- Physician Lead
- Nursing Lead
- Charting Nurse
- RT
- Anesthesia
- Rapid Response/Code Team
- Porter
- MLT – Transfusion Medicine
- MLT – Core lab (Hematology, Coagulation, Biochem)
- OB: back up anesthesia, second call OB, neonatologist, NICU RN
- Chaplain

SMALL Hospital

- Physician Lead
- Nursing Lead
- Charting Nurse
- Code Team
- Anesthesia if available
- Porter
- MLT – Transfusion Medicine and Core Lab
- OB: Obstetrician on call

Team

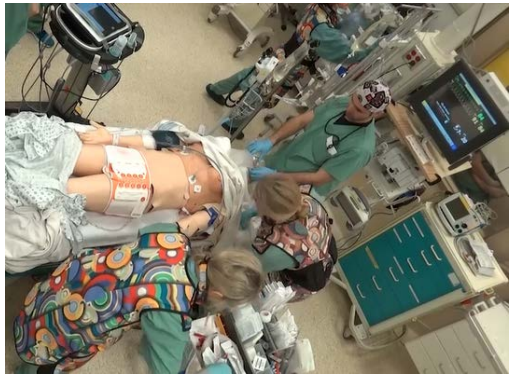
Challenges

- Team members with different levels of experience
- Team members that may not have worked together previously
- Team members that are geographically separated
- Professional silos and hierarchies

Solutions

- Training including simulation and debriefing after each MHP
- Wearing signs with MHP role designation
- Effective communication means
- Regular time-outs
- Smart records and checklists

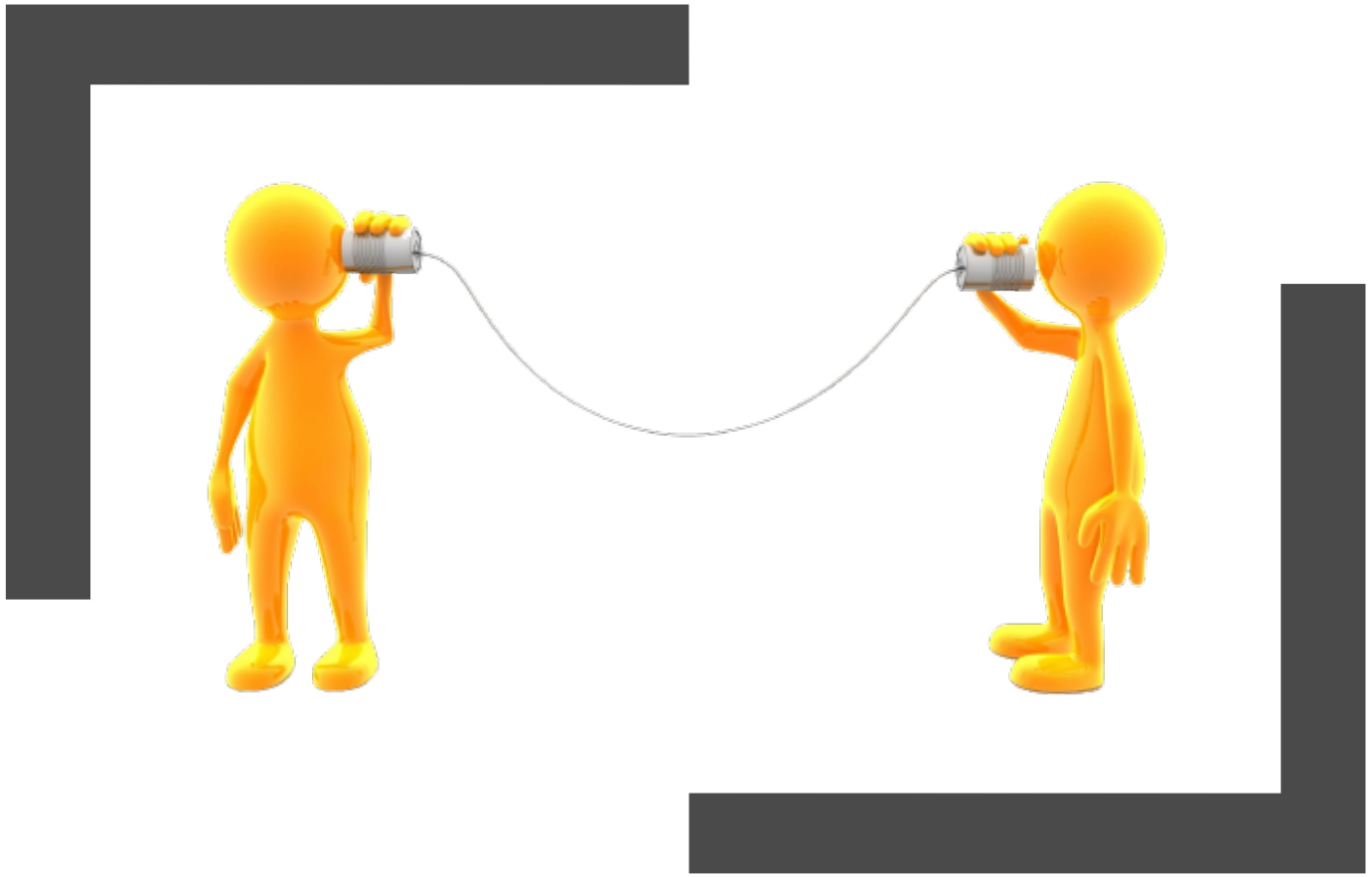
Team Training



- Before training
  - Development and implementation of MHP – must have a functional plan!
  - Plan must contain facilitators (make it easy to do it right)
    - Records, Checklists, Apps
- Training and competency maintenance or assessment
  - Didactic, case-based, simulation
  - Mock codes/drills
    - In situ mock codes significantly improve response times, increase staff confidence levels and are correlated with improved patient survival

Herbers & Heaser Am J Crti Care 2016; Andreatta et al Pediatr Crit Care Med 2011; Oldroyd et al BMC Res Notes 2016

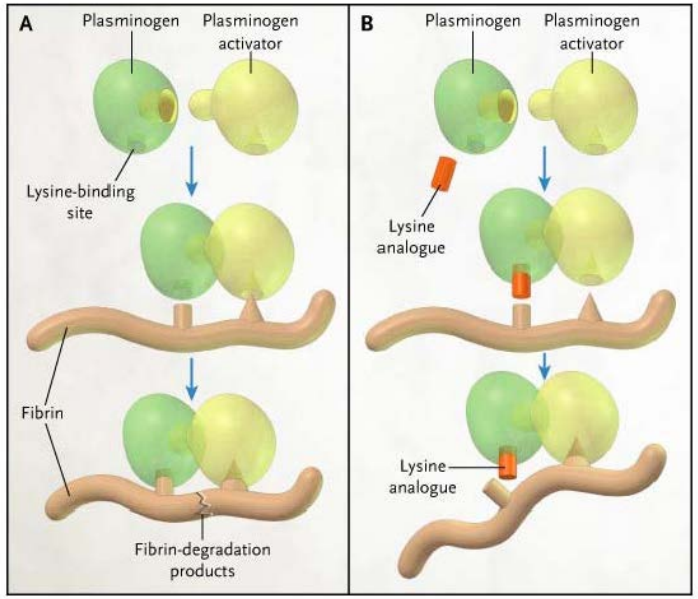
Team Communication



- How? Established, reliable and mobile means to communicate
- Who? MHP clinical team, laboratories, porter, other services
- When? Trigger/terminate, location change, clinical status change, goals of care change, transfer of care

Tranexamic Acid (TXA)

- TXA is an antifibrinolytic
  - stabilizes clot, reduces bleeding, improves mortality
- Give TXA ASAP within the first 3 hours of injury (but if possible <1 hour) in trauma patients and as soon as MHP is called for all other patients
- Dosages and infusion rates may vary
  - 1g bolus plus 1g infusion over 8 h
  - 1g bolus and 1g bolus repeated at 1 h
  - 1g bolus and repeated if ongoing bleeding at ≥ 30 min
  - 2g bolus at the scene of the injury



TXA

- Find out if TXA was already given in the field and how much
- If none given and it is within 3 hours of injury, administer 2g IV bolus
- If 1g given and it is within 3 hours of injury, administer 1g IV bolus

https://www.theglobeandmail.com/life/health-and-fitness/hospitals-shun-cheap-drug-used-to-stop-bleeding/article4178385/

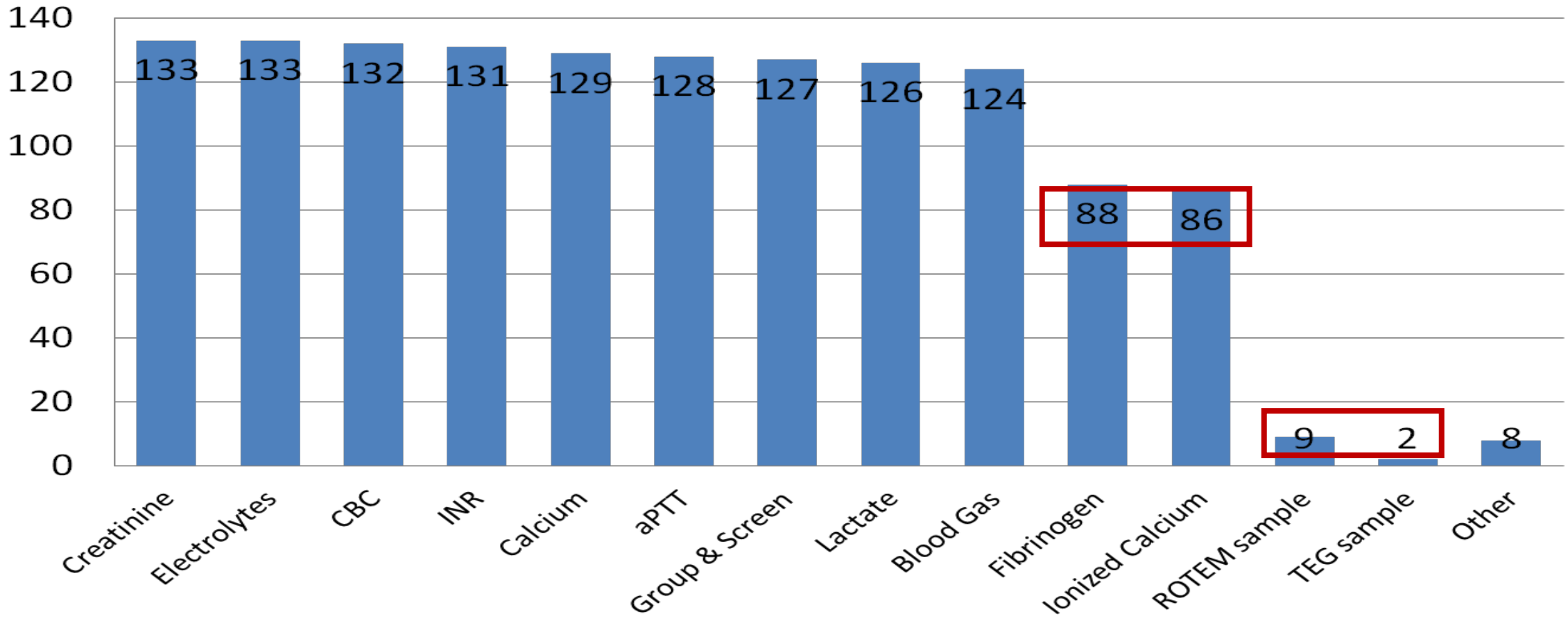
Temperature

- Check temperature within 15 min of MHP activation and then every 30 min or continuously
- Promote normothermia (aim for temperature 36C) by passive and/or active warming
- Use warmer to administer
  - IV crystalloid
  - RBC and Plasma

Testing

- Tests to assess organ damage or adequacy of resuscitation
  - Blood gases, lactate, troponin, creatinine
- Tests to assess Hgb and hemostatic function
  - CBC
  - Standard: INR, aPTT, fibrinogen
  - Specialized: ROTEM/TEG (thromboelastometry)
  - Consider that abnormal test results might be from anticoagulants in older patients
    - aPTT up = dabigatran
    - INR up = warfarin, apixaban, rivaroxaban, edoxaban

ON Survey: Test Availability in Hospitals



Chin et al Injury 2019

Testing

- Should be done at activation/termination and at pre-defined intervals (at least hourly during MHP, prior to each pack, etc.)
- Some hospitals have order sets/bundles and/or prepared packs with tubes and requisitions
- Lab calls (and clinical team should be ready to receive!) critical results

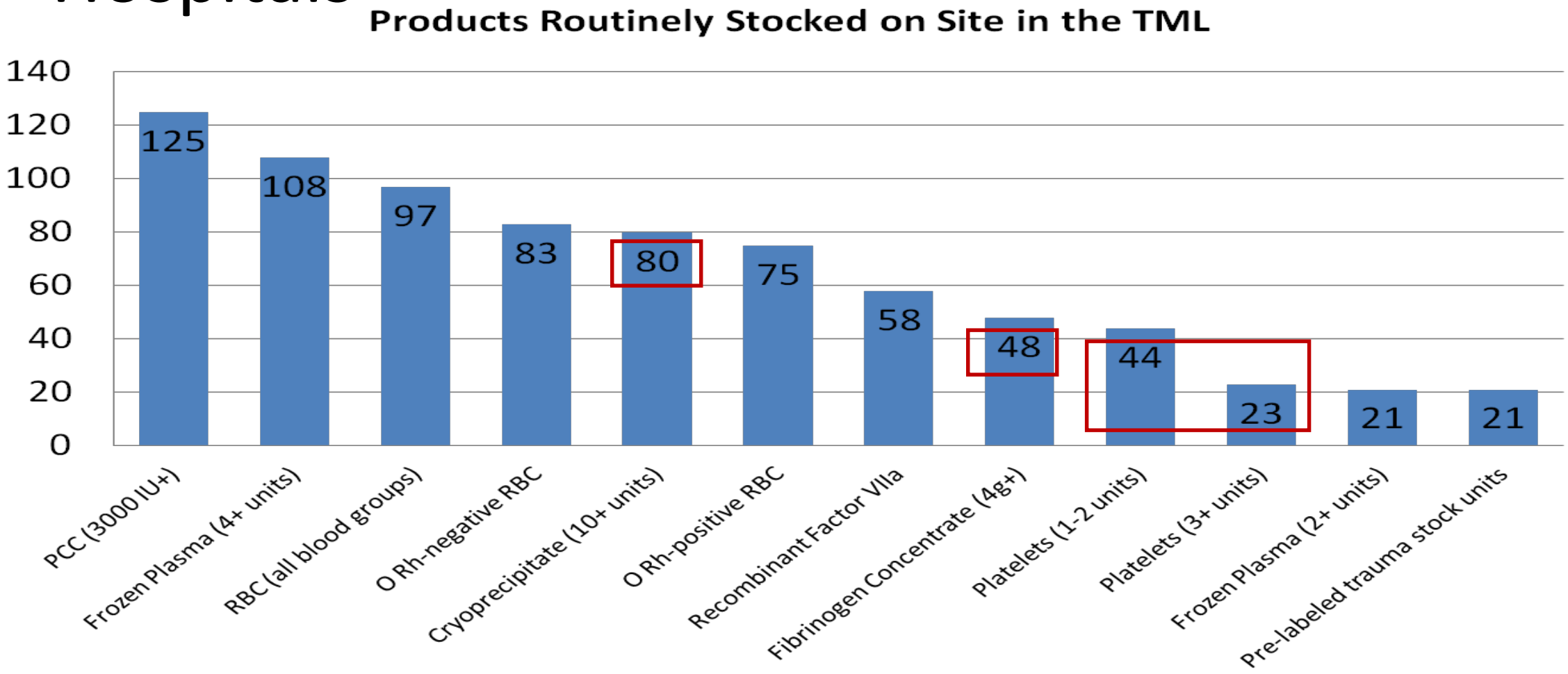
Big Hospital	Small Hospital
CBC (Hgb, PLT)	CBC (Hgb, PLT)
INR, fibrinogen ROTEM	INR, fibrinogen if available
Lactate or ABG/VBG	Lactate or ABG/VBG
Ionized calcium	Calcium
Lytes, Creatinine, Trp	Lytes, Creatinine, Trp

Urgent Reversal of Anticoagulants

Be familiar with antidotes and reversal policies

Drug	Warfarin	Dabigatran	Xa inhibitors (Rivaroxaban, Apixaban, Edoxaban)
Mechanism	Causes vitamin K deficiency	Inhibits IIa	Inhibit Xa
Effect on coagulation testing	Increases PT/INR	May increase aPTT Increases thrombin time and dilute thrombin time	May increase PT/INR Increase Xa
Antidote	Vitamin K PCC (or FP)	Praxbind	No
If no antidote, what can be tried?	N/A	N/A	PCC

ON Survey: Blood Routinely Stocked in Hospitals



Chin et al Injury 2019

Transfusion: Large Hospital

TM Shipments (q30min):

- Box 1 : 4 RBC
- Box 2: 4 RBC , 4 plasma
- Box 3: 4 RBC, 2 plasma, 4g FC
- Box 4+: 4 RBC, 2 plasma

- Transfuse platelets based on platelet count
- Give more FC as per fibrinogen level
- Switch to lab-based transfusion as soon as active bleeding is controlled

RBC

- O Rh negative RBC to females <45 years old and O Rh positive RBC to all others
- Switch to group specific RBC when group determined
- Switch to crossmatched RBC when compatibility testing

Plasma

- AB plasma
- Switch to group specific or compatible plasma when group is known/plasma thawed

Platelets

- Any group

Fibrinogen Concentrate

Transfusion: Small Hospital

TM Shipments

- **Box 1: 4** RBC
- **Box 2: 4 RBC and where plasma not stocked** 2,000IU PCC, 4g FC
- **Box 3 and subsequent**: transport out

- Transfuse platelets based on platelet count

- RBC
  - O Rh negative RBC to females <45 years old and O Rh positive RBC to all others
  - Number of units may vary
- Platelets
  - If not stocked, order
  - If patient is transferred out before platelets are transfused, communicate this to receiving hospital

Transfusion

Component	Transport	Storage at bedside	Blood warmer?
RBC	Cooler (temp controlled)	Cooler	Yes
Plasma	Cooler (temp controlled)	Cooler	Yes
If warm/just thawed	Plastic bag	Bedside, ambient temp	Yes
Platelets	Plastic bag	Bedside, ambient temp	No
Cryoprecipitate	Plastic bag	Bedside, ambient temp	No

Transfusion

- Switch from 2:1 ratio RBC to FP to lab-guided transfusion ASAP to avoid overtransfusion
- **Ontario Provincial MHP Targets**

Laboratory Test	Transfusion
Hemoglobin<80g/L	RBC
INR>1.8	Plasma 15mL/Kg (3-4 units)
Platelets<50	1 adult dose of PLT
Fibrinogen <1.5g/L	Fibrinogen concentrate 4g

Termination

- Termination criteria
  - Hemorrhage is controlled or patient succumbed
- Termination process
- Transfer of care including completion of charting and hand-over
- Return coolers and any unused blood components to transfusion medicine

Termination

- Inform patient and/or their substitute decision maker about MHP
- Discuss risks of massive transfusion
  - Common: fever, rash, TACO, hyperkalemia
  - Uncommon: TRALI
  - Potential Risks (eg. RBC alloimmunization in women of child-bearing potential)
- Women of child-bearing potential should undergo red cell antibody screening at 6 weeks and/or 6 months after transfusion

Tracking Performance

- Tracking performance
  - Audits, mortality and morbidity rounds
  - Utilization review at a multidisciplinary committee
  - Debriefing, huddle
    - Debriefing improves psychological well-being and communication after trauma resuscitation
    - Debriefing improves performance in simulation
    - Structured audiovisual interdisciplinary debriefing improves patient survival
- Benchmarking
  - Ontario Trauma Registry, Trauma Quality Improvement Program TQIP (American College of Surgeons), others

Garden et al Anaesth Intensive Care 2015; Berg et al J Trauma Nurs 2014; Wolfe et al Crit Care Med 2014

Tracking Performance

- Compliance with MHP is not optimal
  - Canadian study:
    - Bawazeer et al: 1.4-94.5% for various interventions
  - American studies
    - Cotton et al: 27% overall protocol compliance
    - Plackett et al: 27-97% for various interventions
      - Significant variability between surgeons

- **Full compliance is an independent predictor of survival**
- **We must strive to do better**

Bawazeer et al Injury 2015; Cotton et al J Trauma 2009; Plackett et al J Trauma Acute Care Surg 2017

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Research

A regional massive hemorrhage protocol developed through a modified Delphi technique

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Abstract

Background: A massive hemorrhage protocol (MHP) enables rapid delivery of blood components in a patient who is exsanguinating pending definitive hemorrhage control, but there is variability in MHP implementation rates, content and compliance owing to challenges presented by infrequent activation, variable team performance and patient acuity. The goal of this project was to identify the key evidence-based principles and quality indicators required to develop a standardized regional MHP.

Methods: A modified Delphi consensus technique was performed in the spring and summer of 2018. Panellists used survey links to independently review and rate (on a 7-point Likert scale) 43 statements and 8 quality indicators drafted by a steering committee composed of transfusion medicine specialists and technologists, and trauma physicians. External stakeholder input from all hospitals in Ontario was sought.

Results: Three rounds were held with 36 experts from diverse clinical backgrounds. Consensus was reached for 42 statements and 8 quality indicators. Additional modifications from external stakeholders were incorporated to form the foundation for the proposed MHP.

Interpretation: This MHP template will provide the basis for the design of an MHP toolkit, including specific recommendations for pediatric and obstetrical patients, and for hospitals with limited availability of blood components or means to achieve definitive hemorrhage control. We believe that harmonization of MHPs in our region will simplify training, increase uptake of evidence-based interventions, enhance communication, improve patient comfort and safety, and, ultimately, improve patient outcomes.

Questions