

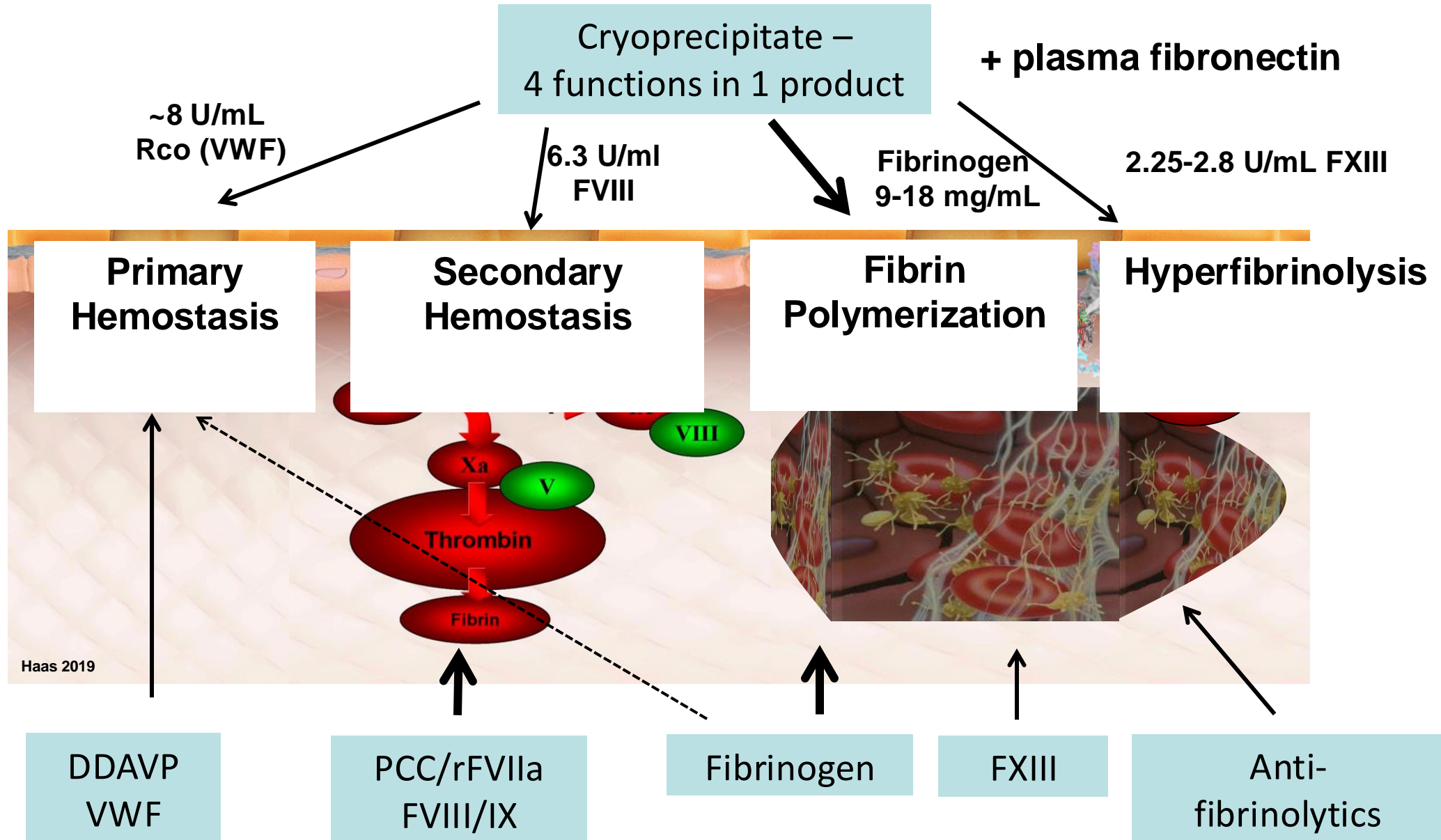
THOR 2019: CRYO

Melissa Cushing, MD

Professor of Pathology and Laboratory
Medicine

Director of Transfusion Medicine
Weill Cornell Medicine, New York City

Bleeding management efficacy using cryo vs factor concentrates

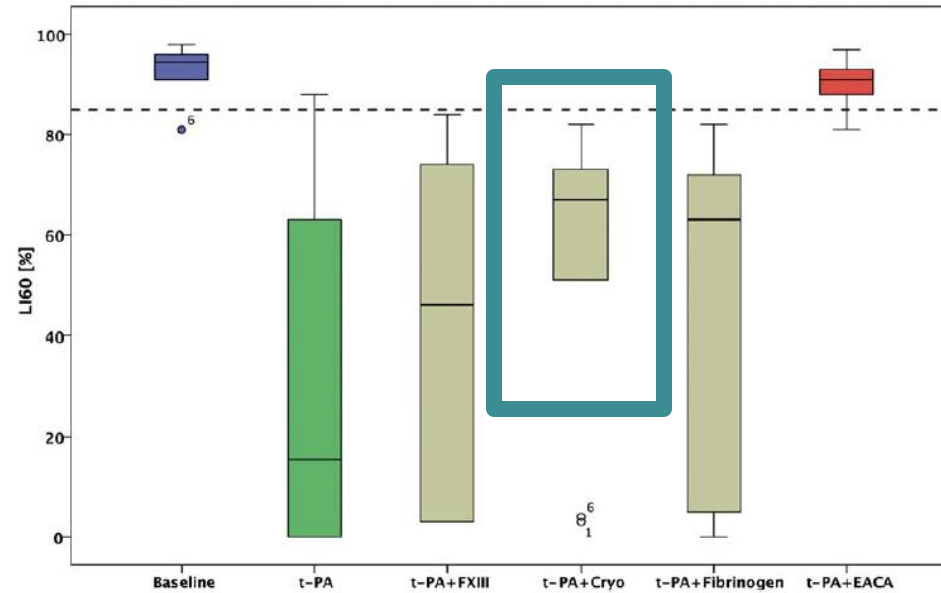


In Vitro Efficacy

Tanaka K, BJA, 2019

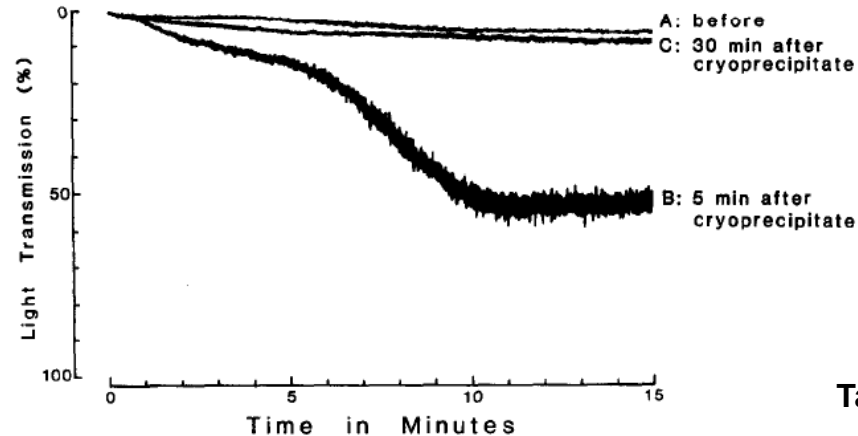
Table 2 Thromboelastometry data

| | INTEM |
|-----------------------|----------------------------|
| | NP |
| Clotting time | 100–240 s |
| Baseline | 164 (155–179) |
| Diluted | 205 (189–218) |
| Diluted+hFC | 205 (188–210) |
| Diluted+Cryo | 188 (183–216) |
| Diluted+vWF/FVIII | 181 (167–216) |
| Maximum clot firmness | 53–72 mm |
| Baseline | 63 (62–66) |
| Diluted | 49 (47–55) |
| Diluted+hFC | 57 [†] (54–61) |
| Diluted+Cryo | 54 [†] (53–60) |
| Diluted+vWF/FVIII | 48 (46–53) |



2) Cryo reverses hyperfibrinolysis better than FC

Cushing M, Transfusion 2017



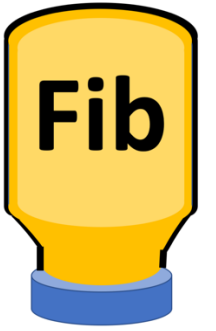
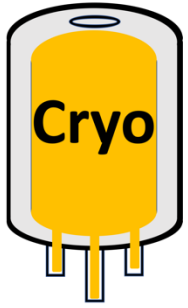
3) Cryo enhances primary hemostasis via platelet aggregation

Takahashi H, Thrombosis Research, 1987

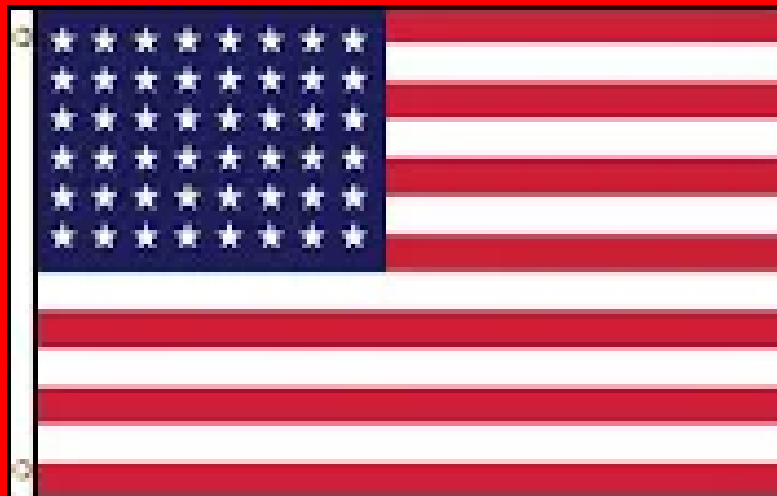
1) Cryo improves thrombin generation better than fibrinogen concentrate

Clinical Efficacy: Systematic Review of Fibrinogen Concentrate vs Cryo

- **4 studies:**
 - **1 RCT in elective cardiac surgery (Galas et al) (n=63)**
 - **3 observational trials (n=218)**
- **Findings:**
 - **Mortality not reported in any study**
 - **No significant difference in:**
 - **Increase in fibrinogen level**
 - **Bleeding**
 - **RBC transfusions**
 - **Thromboembolic complications**
- **Pending studies: FIBRES and FEISTY**



Make Cryo Great Again!



| |
|--------|
| 2018 |
| At La |
| Acad |
| Tertia |
| Centr |
| Trans |
| Wast |
| Total |

| |
|-----------------|
| ratio |
| cost: x cryo |
| cost: x cryo |

14/g



FIBRINOGEN CONCENTRATE IS THE FUTURE

**Logistics
Safety**



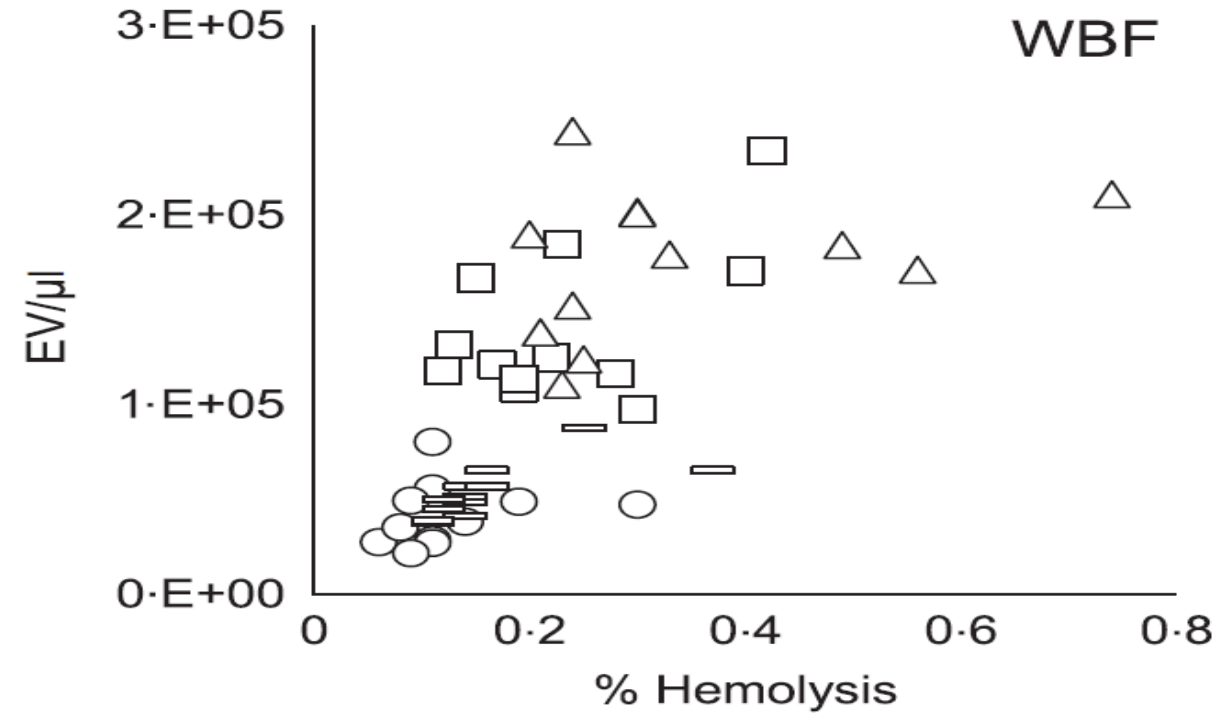
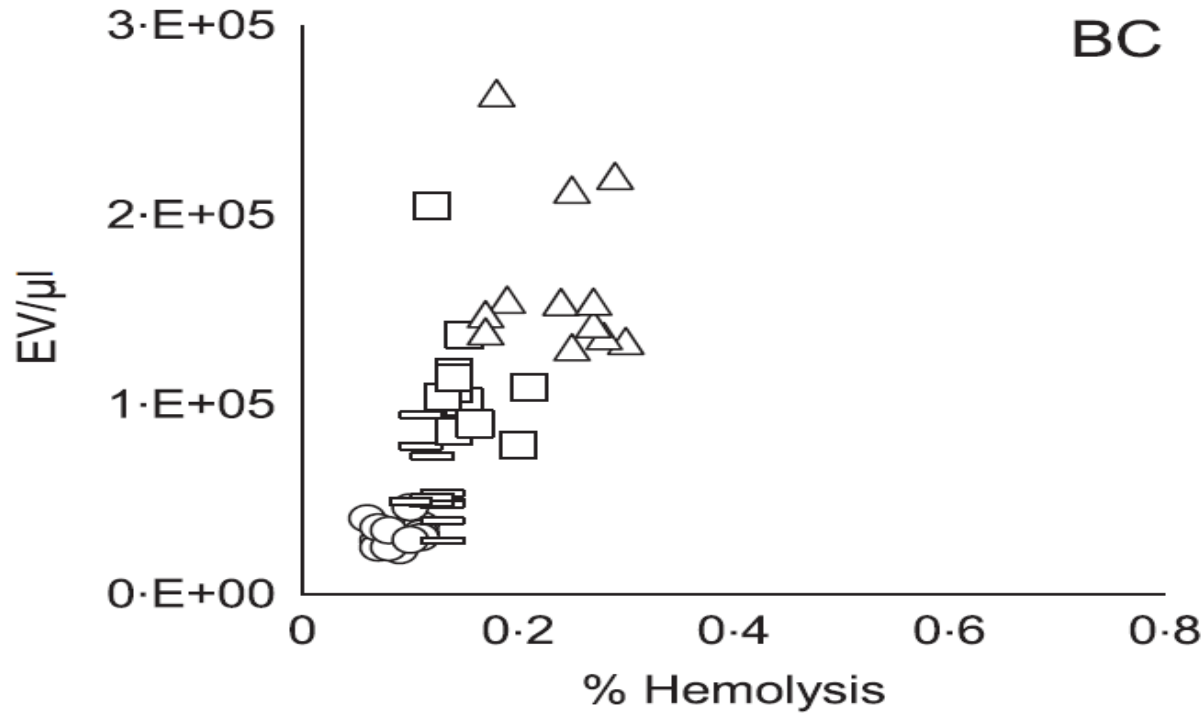
**Jeannie Callum, MD, FRCPC
Director of Utilization, LMMD
Professor, UoT**

91,065 RBC transfusions were given to 23,634 adults

LOGISTICS

Loss of platelets and

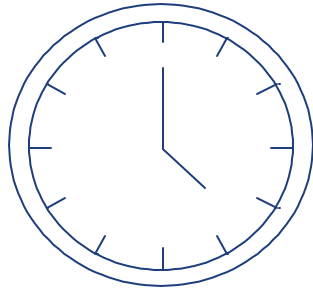
Old red cell filtered



○ d5, — d14, □ d28, Δ d42

LOGISTICS

- ⊙ Hospitals = freezers; manpower intensive; slow; high wastage
- ⊙ Bedside = a long wait in an exsanguinating patient



MINUTES MATTER

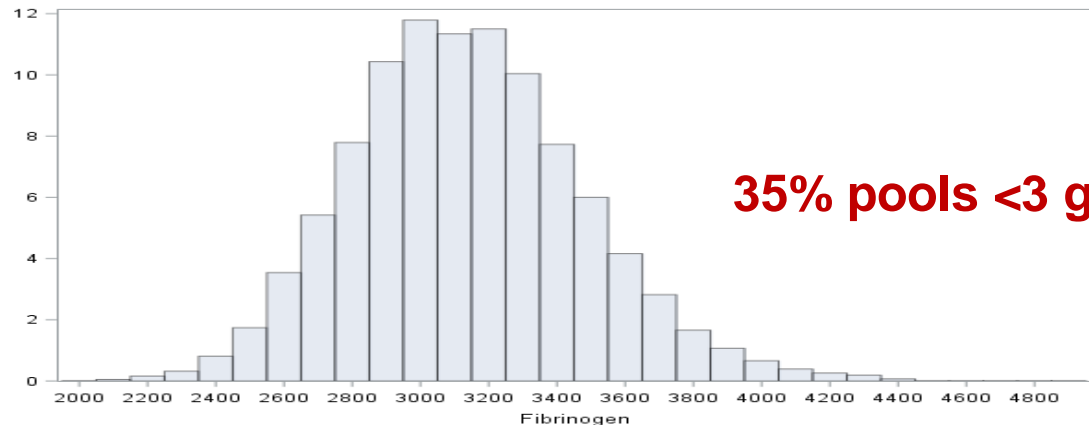
SAFETY

Prevention will be cheaper

- ⊙ Emerging pathogens
- ⊙ “Escaping” pathogens
- ⊙ Risks to the MDs making this decision
- ⊙ Other factors in cryo increasing the clot risk
- ⊙ 35% of the time <3g
- ⊙ Hemostatic efficacy



Distribution of s



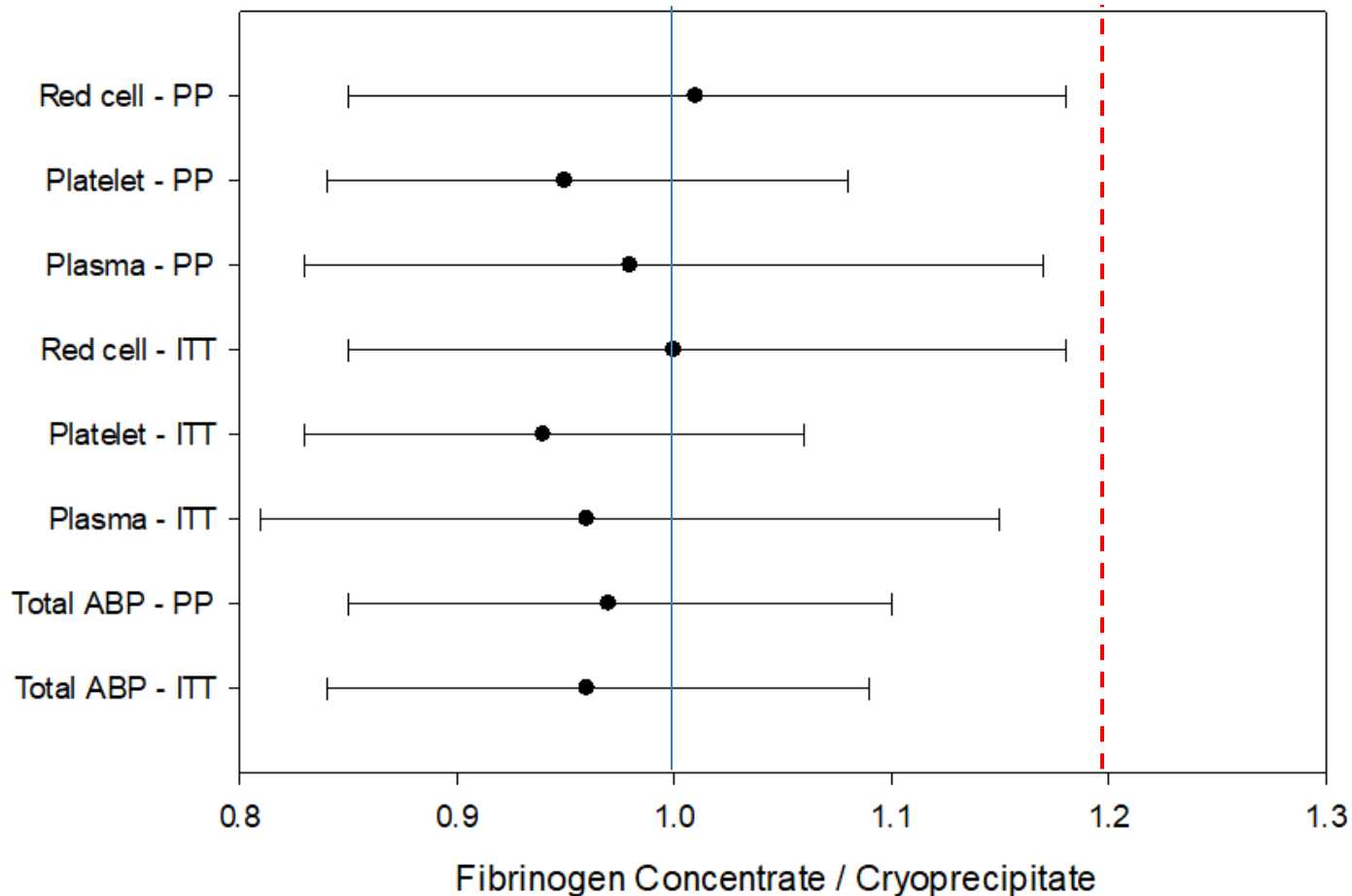
35% pools <3 grams

**FIBRES
Trial**

Cardiac Surgery

735 patients

**Superior for elective
surgery
OR 0.81
(0.69-0.96)
n=466**



Optimized Fibrinogen Replacement Product



Standardized dose for fibrinogen & FXIII ✓

Pathogen Inactivated ✓

Immediately Available/Longer Shelf Life ✓

Stored at Room Temperature ✓

Highly concentrated/Minimal Volume ✓

Limit level of FVIII ✓

Fast and simple infusion ✓

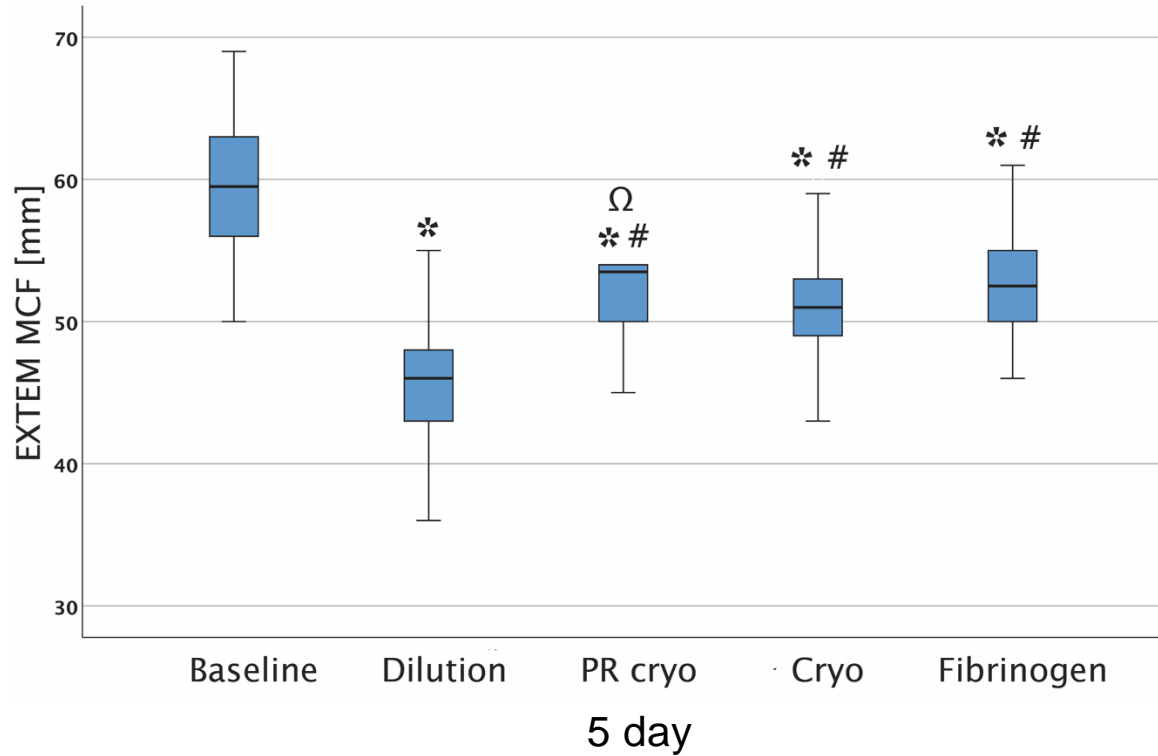
**Make Cryo
Great
Again!**

A small icon of the United States flag.

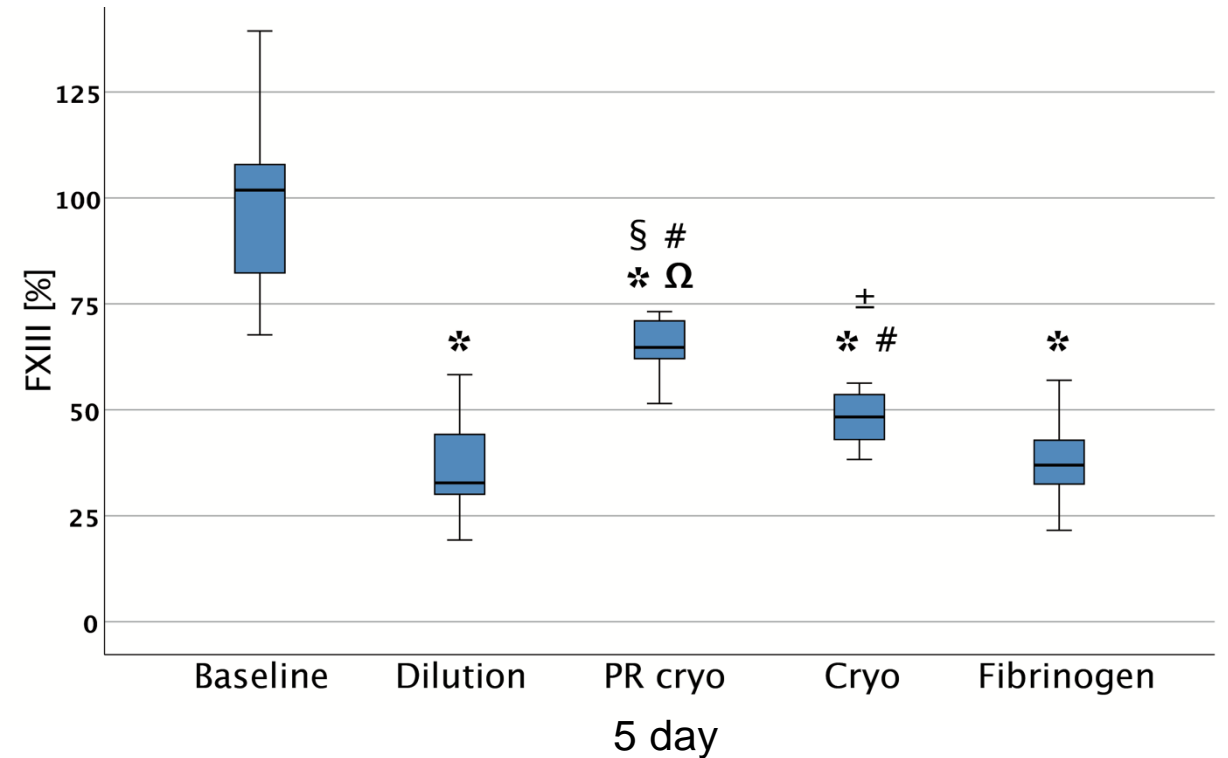
**And
Affordable!**

Pathogen Reduced Cryoprecipitate Thawed and Stored for 5 days at RT

EXTEM



FXIII Activity



Summary

grab 'n go?



5 day PR Cryo

VS



Fibrinogen Concentrate



QUESTION: LYOPHILIZED CRYOPRECIPITATE?



Jeannie Callum, MD, FRCPC
Director of Utilization, LMMD
Professor, UoT

LYOPHILIZED CRYO

NO!

- ⊙ Not pathogen reduced
- ⊙ 35% suboptimal dose
- ⊙ Fractionators have more than enough fibrinogen than we could ever need (IVIG/SCIG drive fractionation)
- ⊙ Technologists concerns regarding ABO incompatibility
- ⊙ Concern about the increase risk of thromboembolic complications from the contaminants in cryo

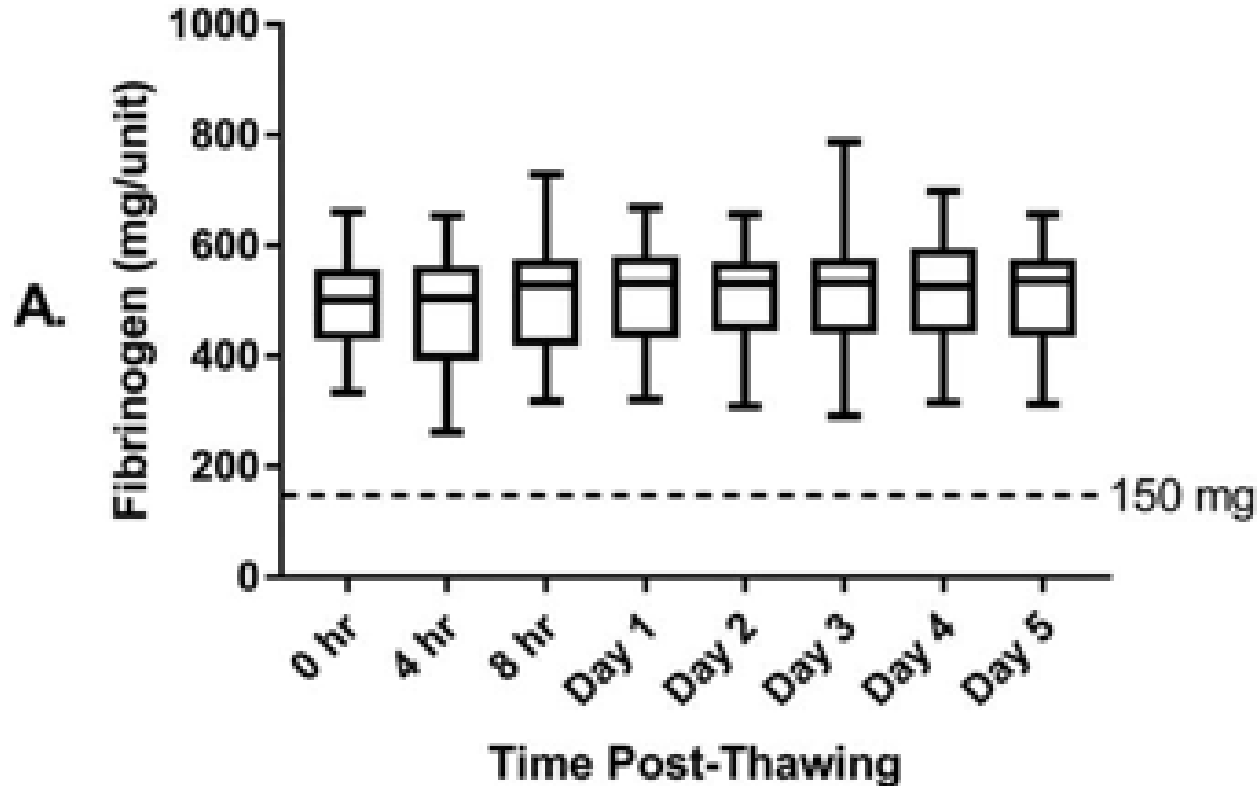
TABLE 1. Comparison of coagulation measurements in blood products

| Measurement | Standard Cryo | PR Cryo | Fibrinogen concentrate |
|--------------------------------|------------------|---------|---------------------------|
| Fibrinogen activity (mg/dL) | 864 | 948 | 1616 |
| VWF:Ag (%) | 904 | 663 | 346 |
| VWF:Rco (%) | 593 | 459 | 104 |
| Factor VIII (%) | 410 | 99.6 | 11 |
| Factor XIII (%) | 224 | 269 | 48 |

VWF:Ag = von Willebrand factor antigen assay; VWF:RCo = von Willebrand factor ristocetin cofactor activity.

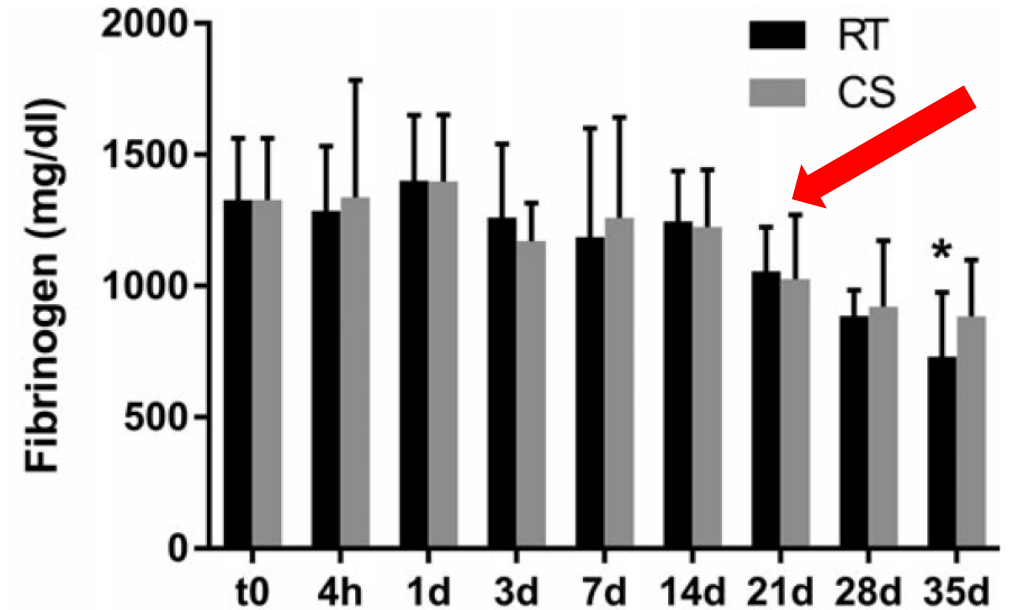
Stability of fibrinogen in Cryo after thawing at RT

120 hours



Lokhandwala, Transfusion, 2018

14 days



Fenderson, Transfusion, 2019

What is in Cryoprecipitate? Do we need it all?

| Protein | Approximate Amount |
|------------------------------|---------------------------------|
| Fibrinogen | ~250-350 mg (min 150 mg) |
| Factor VIII | > 80 IU |
| Von Willebrand Factor | 80-120 IU |
| Factor XIII | 40-60 IU |
| Fibronectin | Unknown |

Economic Evaluation Cryoprecipitate versus Fibrinogen Concentrate

- **Assumptions:**
 - **Cost of Cryo dose (5 units) - \$322**
 - **Cost of FC dose (1 gram) - \$740**
 - **Wastage rate of Cryo – 28%**
- **Results:**
 - **Without considering cryo wastage: FC is \$1254-1672 more per dose**
 - **After taking into account wastage and technologist's salary (\$25/h), FC was \$976-1303 more expensive than Cryo**
 - **To be economically competitive with Cryo, FC would have to cost \$414/g**

FXIII

Haas T, Cushing M, Asmis L, Scandinavian J of Clin and Lab Investigation

Table 3. Comparison of plasmatic coagulation measurements following *in vitro* supplementation using Haemocomplettan and Fibryga.

| Measurement | Haemocomplettan | Fibryga | <i>p</i> value |
|---|-----------------|-------------|----------------|
| Clauss (g L ⁻¹) | 1.76 (0.14) | 1.65 (0.14) | <.001 |
| Fibrinogen antigen (g L ⁻¹) | 1.90 (0.17) | 2.02 (0.18) | .026 |
| Fibronectin (g L ⁻¹) | 0.08 (0.02) | 0.02 (0.01) | <.001 |
| Factor XIII (%) | 31.0 (6.2) | 40.9 (6.2) | <.001 |

Data are presented as mean (SD).

Fibryga 10.1 U/mL FXIII
Haemocomplettan 7.2 U/mL FXIII