Studying Whole Blood Resuscitation

the SWAT and the PPOWER study

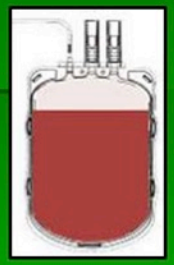
THOR meeting

Bergen, Norway

June 17-20th, 2018

Why Whole Blood

1:1:1 Component Therapy



Component Therapy:

1U PRBC + 1U PLT + 1U FFP + 1 U cryo

680 COLD mL

- *Hct 29%*
- *Plt 80K*
- *Coag factors 65% of initial concentration*
- *1000 mg Fibrinogen*

•Armand & Hess, Transfusion Med. Rev., 2003

WWB:

500 mL Warm

Hct: 38-50%

Plt: 150-400K

Coag: 100%

1000 mg Fibrinogen

Why Whole Blood

PROPPR

Pragmatic, Randomized Optimal Platelet and Plasma Ratios

Original Investigation

Transfusion of Plasma, Platelets, and Red Blood Cells in a 1:1:1 vs a 1:1:2 Ratio and Mortality in Patients With Severe Trauma

The PROPPR Randomized Clinical Trial

John B. Holcomb, MD; Barbara C. Tilley, PhD; Sarah Baraniuk, PhD; Erin E. Fox, PhD; Charles E. Wade, PhD; Jeanette M. Podbielski, RN; Deborah J. del Junco, PhD; Karen J. Brasel, MD, MPH; Eileen M. Bulger, MD; Rachael A. Callcut, MD, MSPH; Mitchell Jay Cohen, MD; Bryan A. Cotton, MD, MPH; Timothy C. Fabian, MD; Kenji Inaba, MD; Jeffrey D. Kerby, MD, PhD; Peter Muskat, MD; Terence O'Keeffe, MBChB, MSPH; Sandro Rizoli, MD, PhD; Bryce R. H. Robinson, MD; Thomas M. Scalea, MD; Martin A. Schreiber, MS; Deborah M. Stein, MD; Jordan A. Weinberg, MD; Jeannie L. Callum, MD; John R. Hess, MD, MPH; Nena Matijevic, PhD; Christopher N. Miller, MD; Jean-Francois Pittet, MD; David B. Hoyt, MD; Gail D. Pearson, MD, ScD; Brian Leroux, PhD; Gerald van Belle, PhD; for the PROPPR Study Group

Why Not Whole Blood

What we need:

- Change beginning to happen
- Determine potential benefits
- Demonstrate to stake holders
- Major Change in Standard Care

Outline

- Whole Blood program at University of Pittsburgh
- Hypothesized Potential Benefits
- LITES network- SWAT study
  Shock, Whole Blood, Assessment of TBI
- R34 NHLBI- PPOWER trial
  Pragmatic, Prehospital, group O, Whole blood Early Resuscitation trial

University of Pittsburgh WB program

- Dr. Mark Yazer, MD / Dr. Darrell Triulzi, MD
- Dr. Alan Murdock, MD
- Dr. Lou Alarcon, MD

Pittsburgh WB Program

- **Blood type and %'s**
  - O-positive: 38 percent
  - O-negative: 7 percent
  - A-positive: 34 percent
  - A-negative: 6 percent
  - B-positive: 9 percent
  - B-negative: 2 percent
  - AB-positive: 3 percent
  - AB-negative: 1 percent

Pittsburgh WB program

- **WB product- Low Titer (< 50), Leuko-reduced, Platelet replete (Terumo system), Group O+ WB**
- **Urgent release from ED fridge**
- **Utilizing 14 day shelf life; recycle to prbcs**
- **Monitor hemolysis**

University of Pittsburgh

Initial safety and feasibility of cold-stored uncrossmatched whole blood transfusion in civilian trauma patients

Mark H. Yazer, MD, Byron Jackson, MD, Jason L. Sperry, MD, Louis Alarcon, MD, Darrell J. Triulzi, MD, *and* Alan D. Murdock, MD, *Pittsburgh, Pennsylvania*

N=47; safe

2 units

University of Pittsburgh

Measurement of haemolysis markers following transfusion of uncrossmatched, low-titre, group O+ whole blood in civilian trauma patients: initial experience at a level 1 trauma centre

J. N. Seheult,[1] D. J. Triulzi,[1,2] L. H. Alarcon,[3] J. L. Sperry,[3] A. Murdock[3] & M. H. Yazer[1,2]

[1]*Department of Pathology,* [2]*The Institute for Transfusion Medicine, and* [3]*Department of Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania, USA*

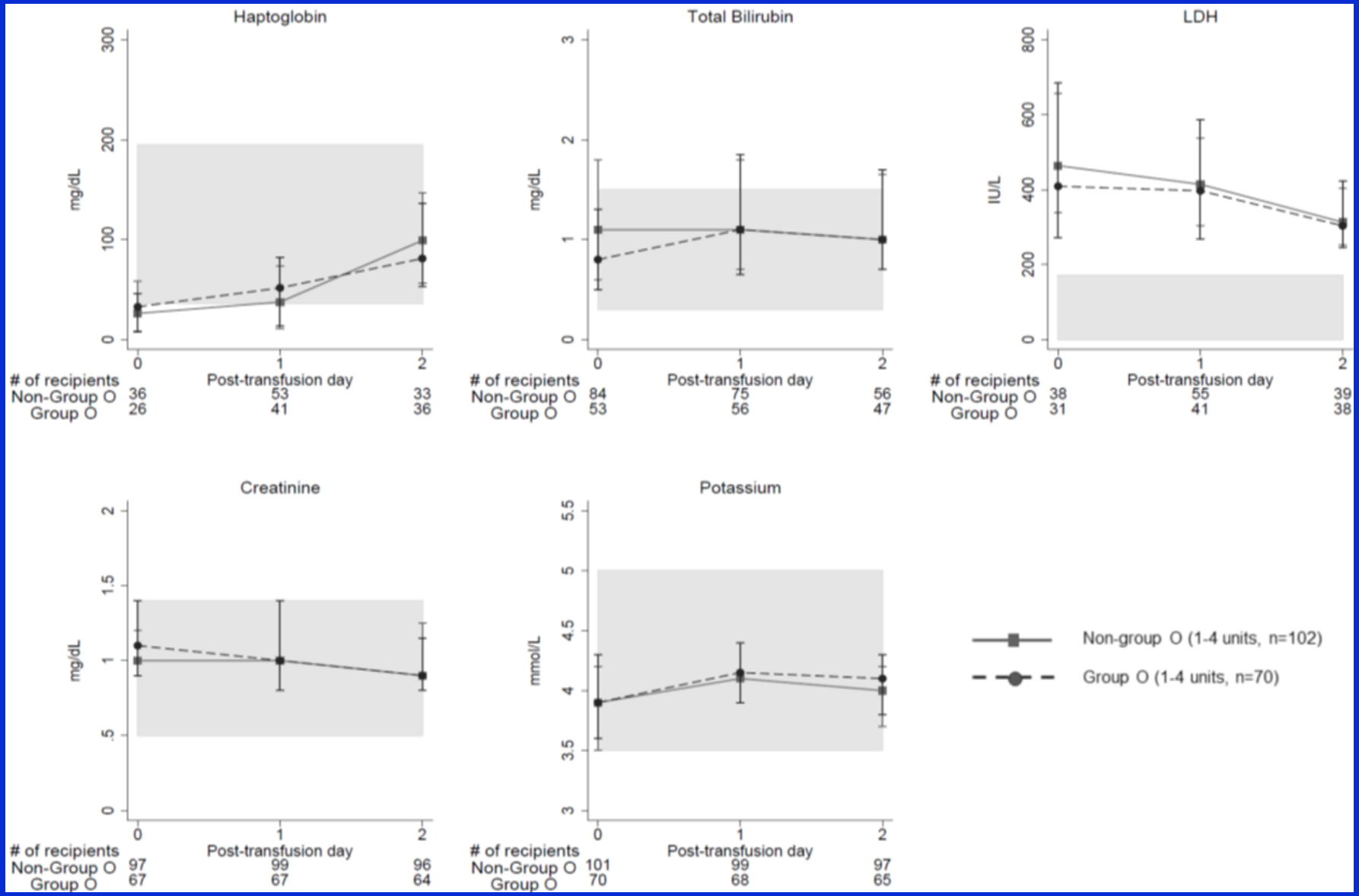
N=44

27 Non-group O recipients

Pittsburgh WB program

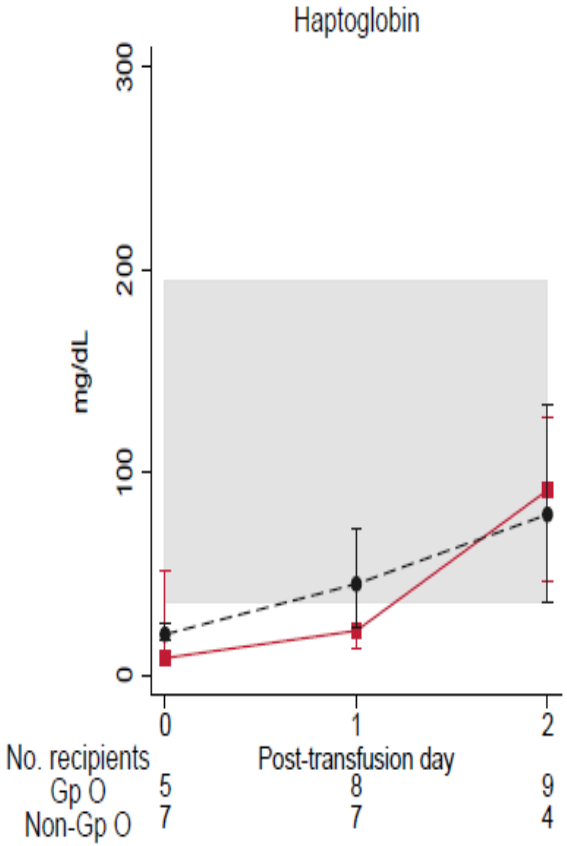
- N=132 in propensity score analysis *in press*;
- Over 275 pts total
- Deemed Safe by Transfusion committee
- Two units ➡ 4 units ➡ 6 units

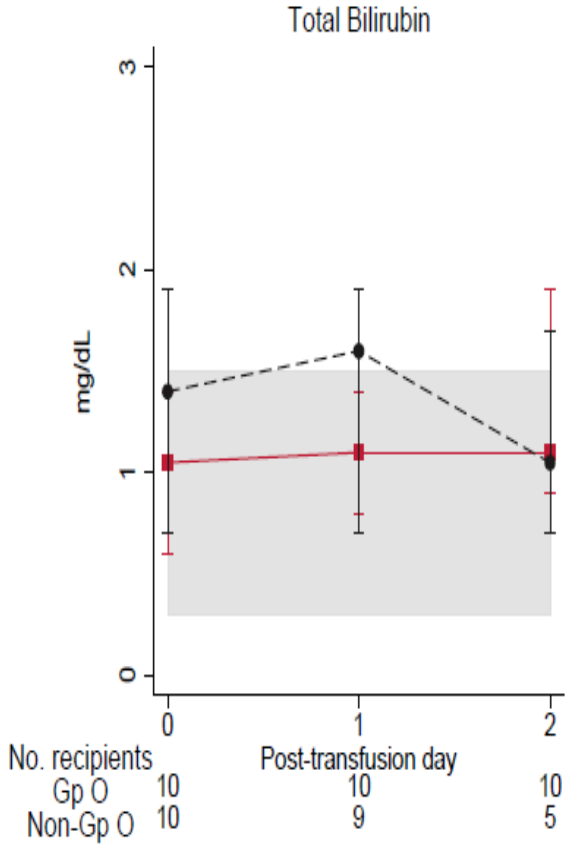
Hemolysis all patients

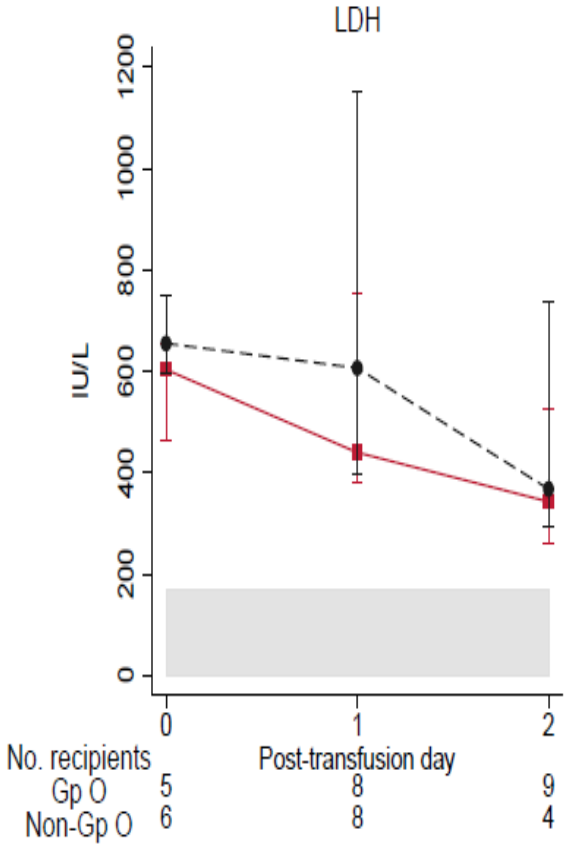


Seheult et al. *Transfusion* in press

Hemolysis in 3 or 4 units WB



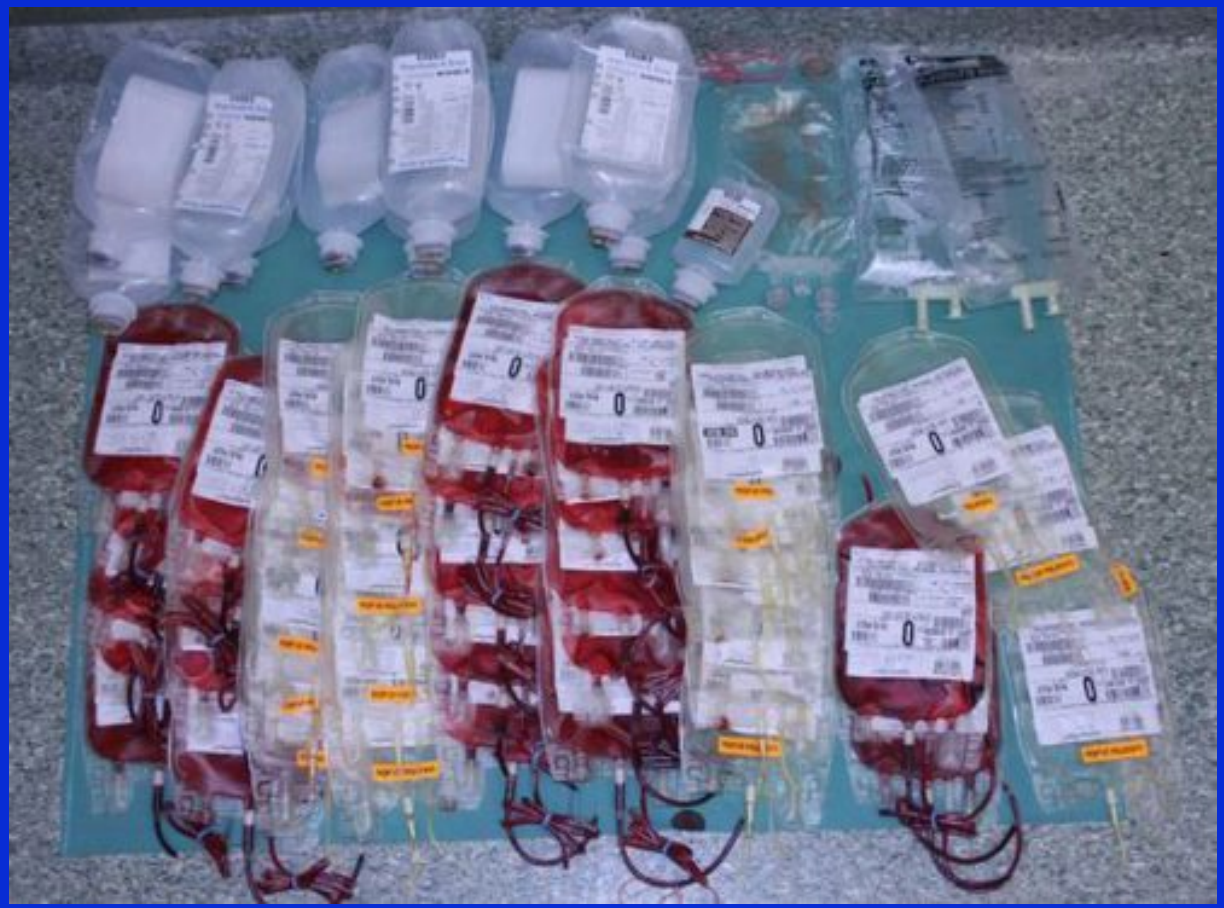




Seheult et al. *Transfusion* in press

Potential Benefits

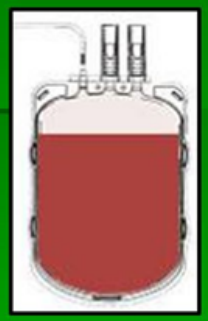
- Ease/Time of Administration



Potential Benefits

- Volume- Less Extra Stuff

1:1:1 Component Therapy



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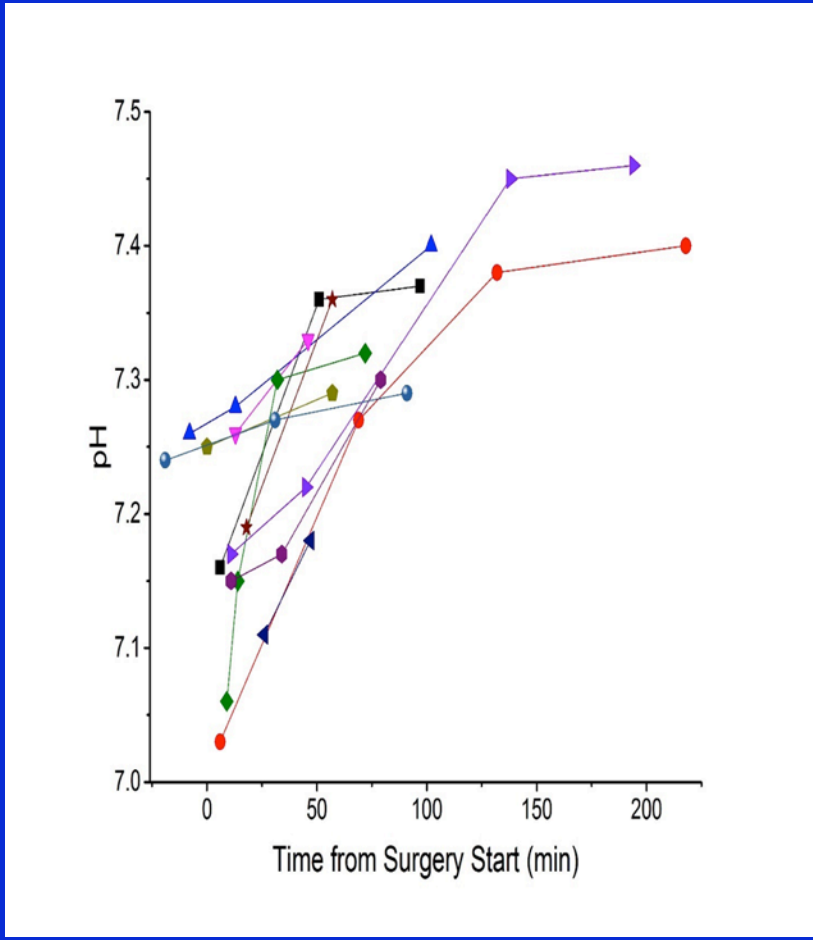
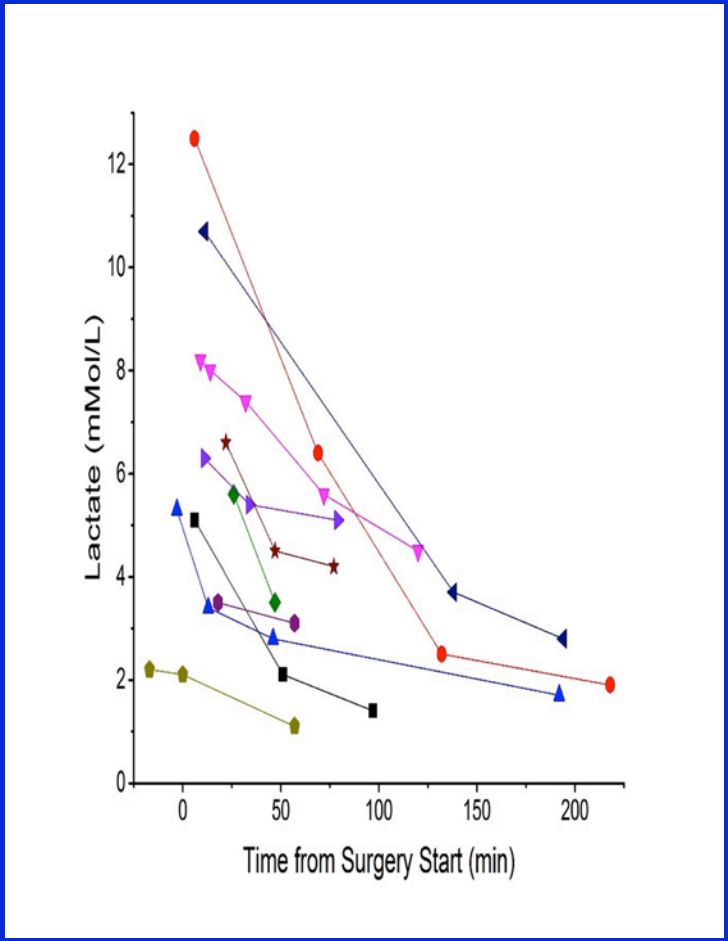
Potential Benefits

- Shock Correction



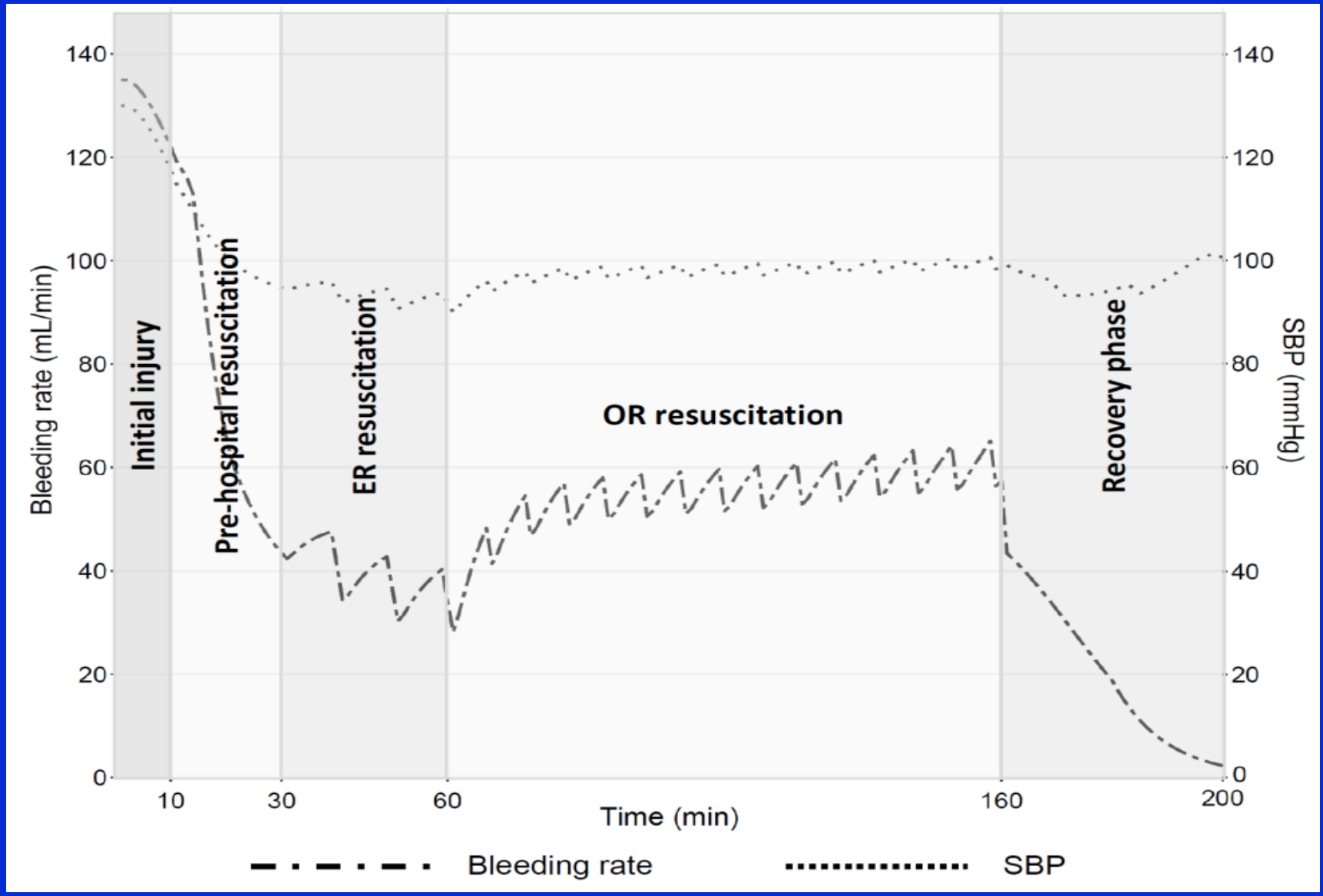


Potential Benefits

Urgent Release capabilities; Time to whole blood

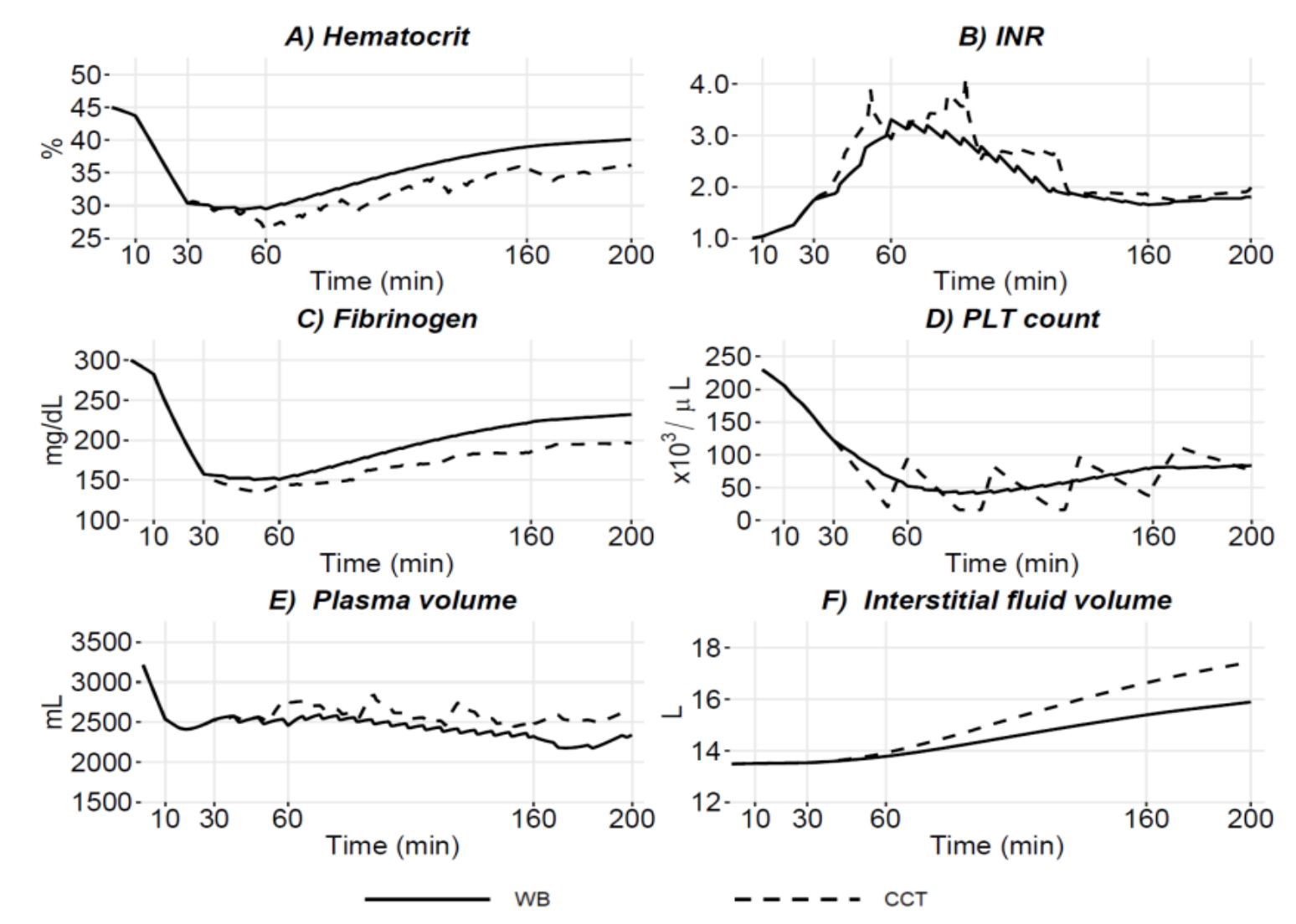
Potential Benefits

In Silico Model-*Submitted* - *Jansen Seheult et al.*



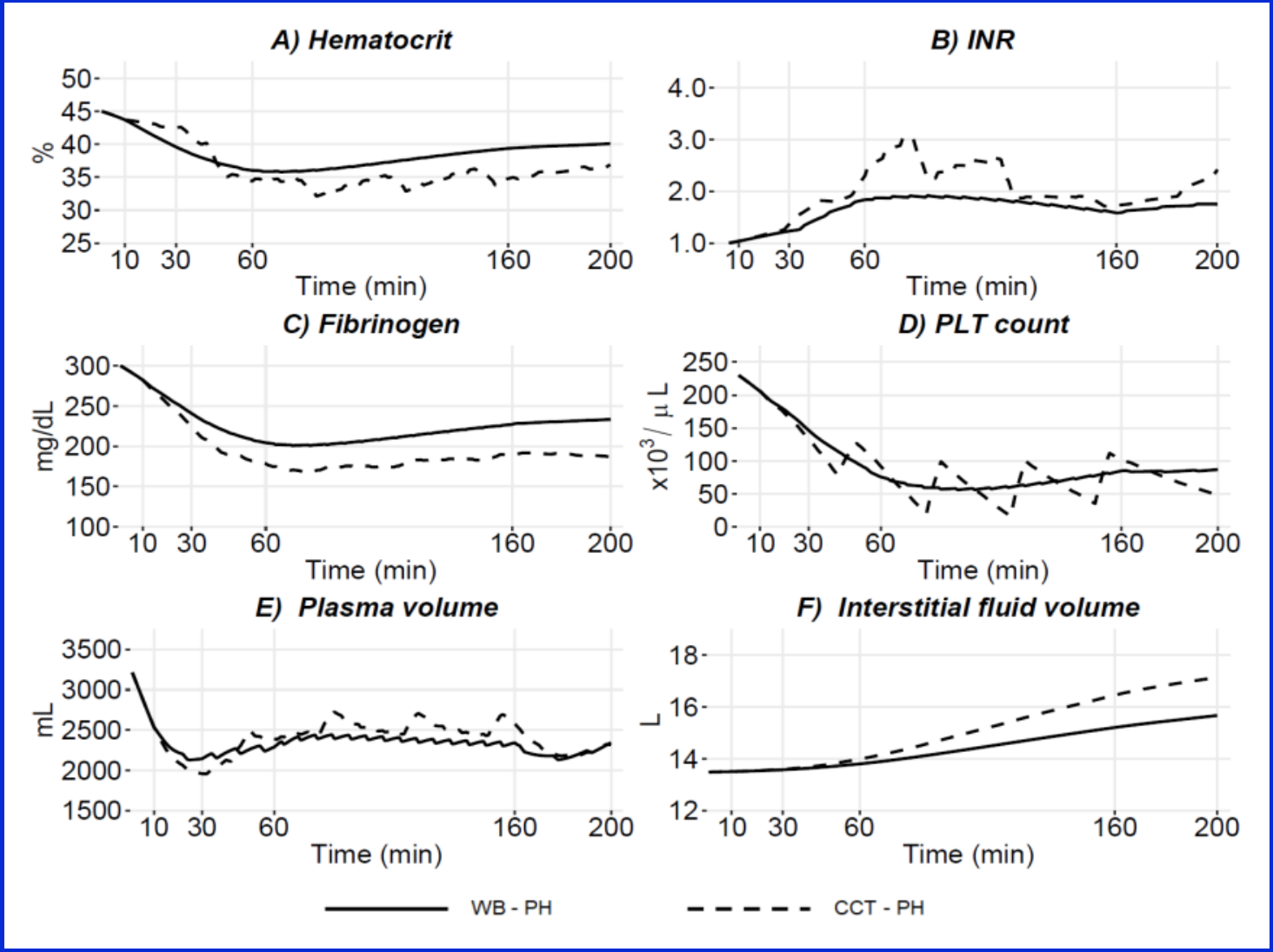
Potential Benefits

Simulation – WB vs CCT



Potential Benefits

Simulation Modeling- WB-PH vs. CCT-PH



LITES Network

Core Trauma Centers

University of Pittsburgh

University of Colorado

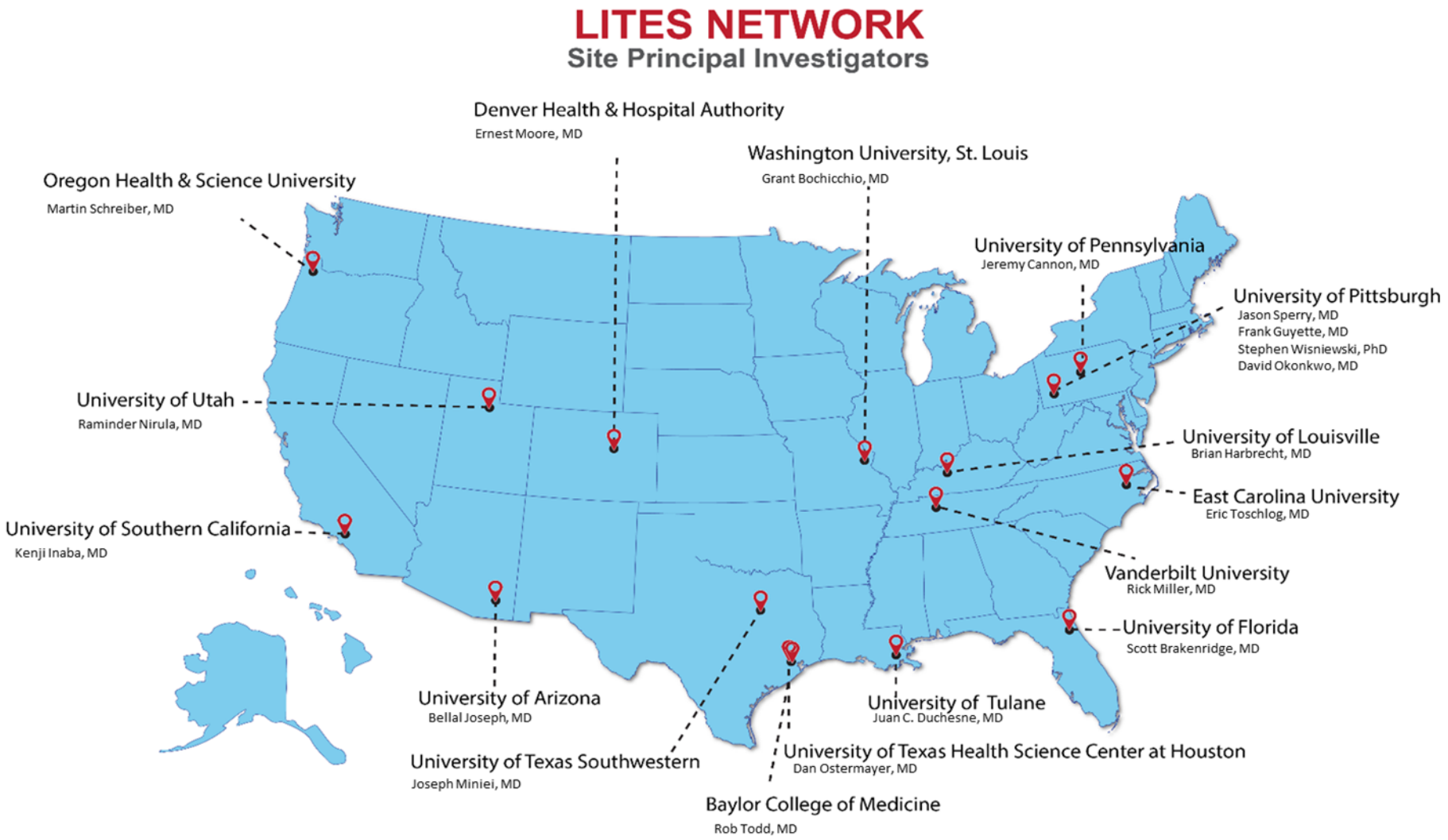
Oregon Health & Science University

Network Capabilities

- Efficient and Capable
- Expandable
  - Multiple Task Orders
  - Variable Interventions/Study Types
- Spectrum of Injury Characteristics-
  - Blunt/Penetrating, Air/ground
- Past experience-
  - PAMPer, STAAMP, COMBAT, PROPPR, ROC, ROC-TXA, TRACK-TBI, Gluegrant
- Central IRB; EFIC thru Long term outcomes

LiTES

LITES Network



LITES Network

Task Order #1-prehospital thru ICU intensive data

Task Order #2- SWAT

Task Order #3-Freeze Dried Plasma

Task Order #4-Cold Stored Platelets

Task Order #5-Prehospital Supraglottic Airway

LITES Network - SWAT

- **Task Order #2 – SWAT**
  Shock, Whole blood, and Assessment of TBI

General Hypothesis #1: Whole blood resuscitation will be associated with improved mortality and resuscitation outcomes in poly-trauma patients and long term neurological outcome in those patients with traumatic brain injury as compared to those resuscitated with component therapy.

LITES Network - SWAT

- **Task Order #2 – SWAT**
  Shock, Whole blood, and Assessment of TBI
- **Prospective observational study**
- **4 years; N=895 patients**
- **6 sites; 3 WB sites and 3 component sites**

LITES Network - SWAT

Inclusion Criteria: Blunt or penetrating injury

1) **Has ABC criteria:**
    a. **Hypotension**
    b. **Penetrating mechanism,**
    c. **Positive FAST abdominal ultrasound,**
    d. **Heart Rate ≥ 120**

AND

2) **Taken to the OR / IR within 60 minutes of arrival.**

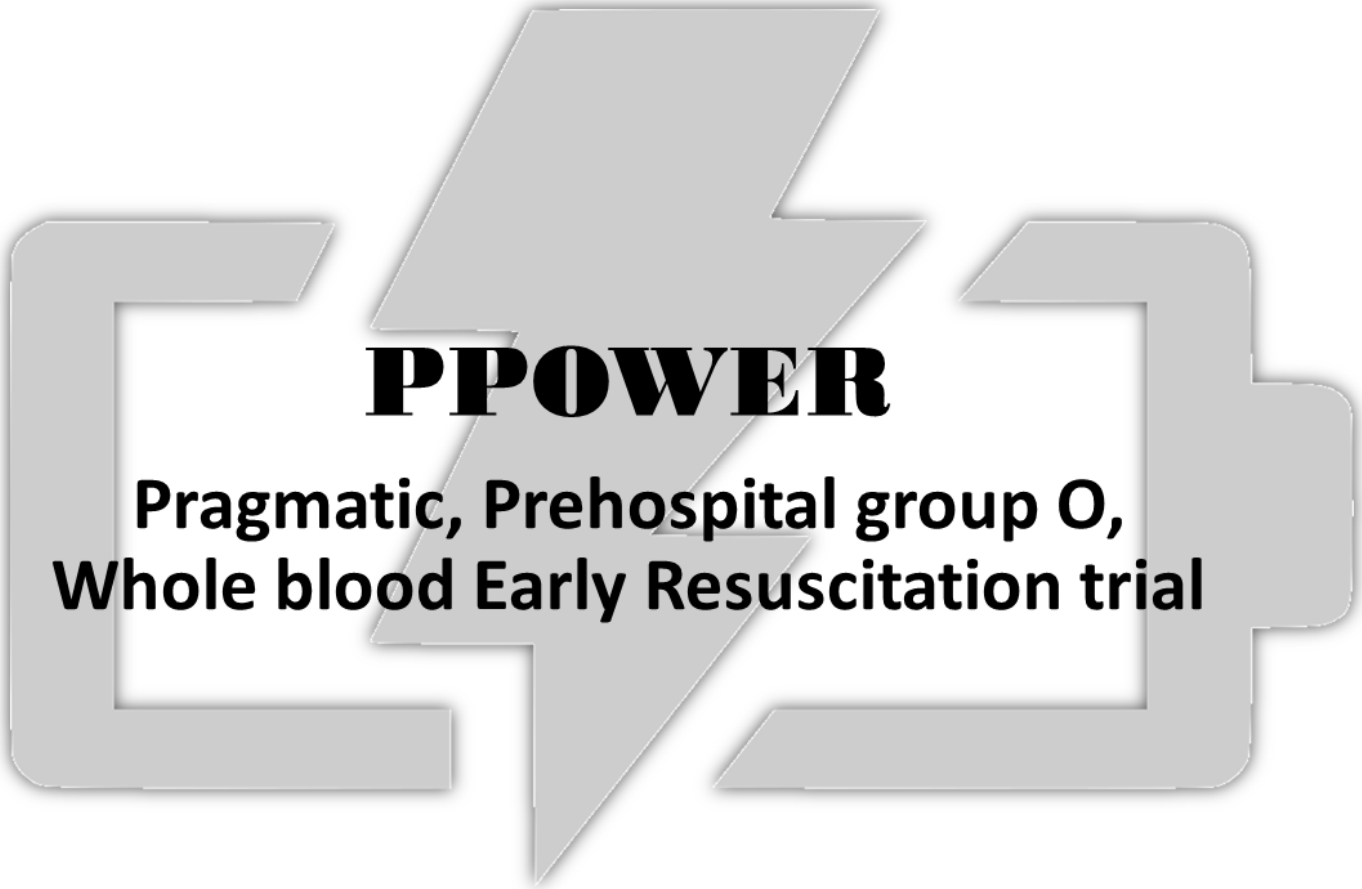
AND

3) **Need of blood/blood component transfusion within 60 minutes of arrival.**

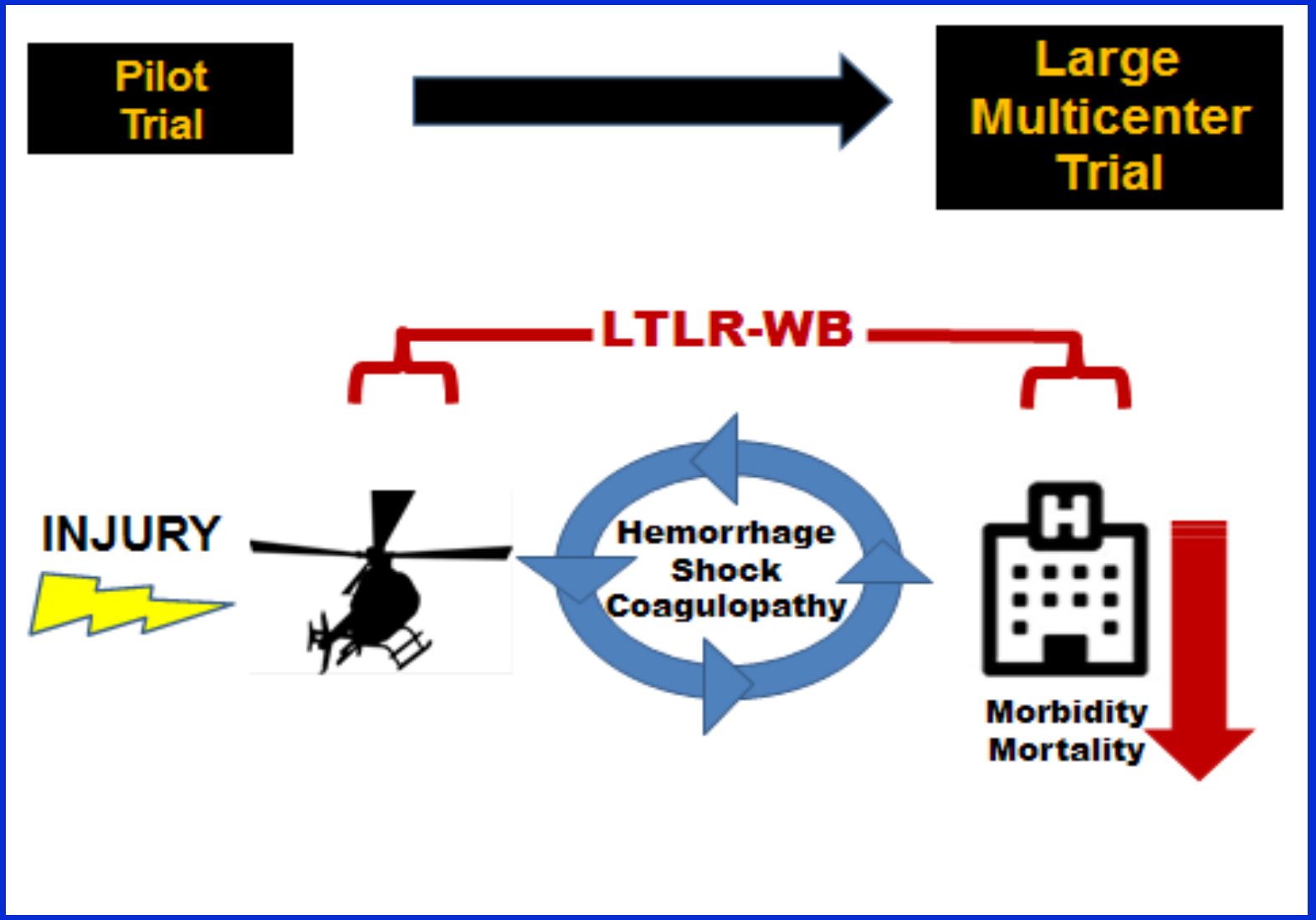
LITES Network - SWAT

- Focus on time to hemostasis, reversal of shock, early mortality endpoints (4hr)
- Intensive early data collection
- TBI imaging and 6 month outcomes

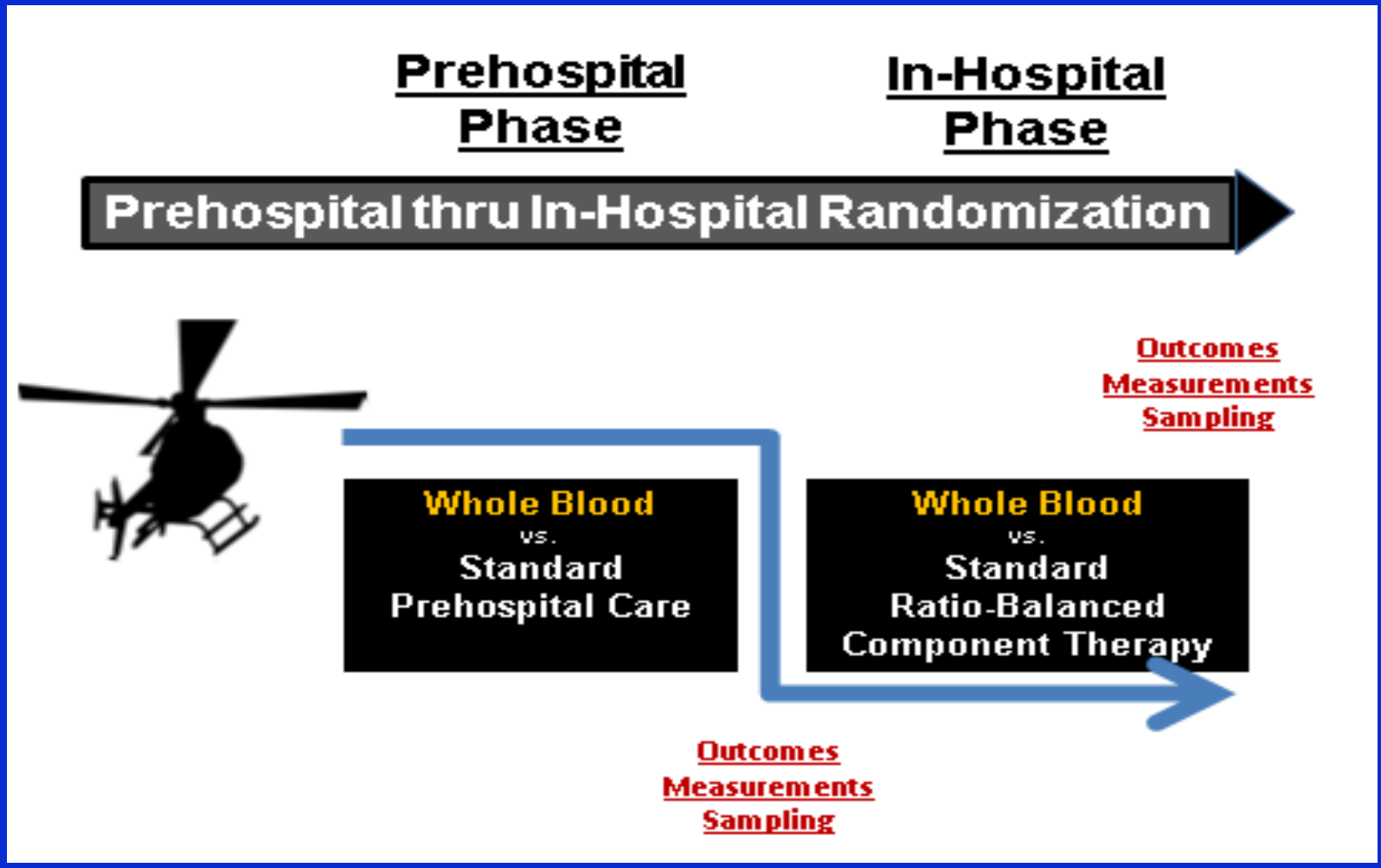
R34 NHLBI Pilot Trial



R34 NHLBI Pilot Trial



PPOWER


Prehospital Phase
In-Hospital Phase
Prehospital thru In-Hospital Randomization
Outcomes
Measurements
Sampling
Whole Blood
vs.
Standard
Prehospital Care
Whole Blood
vs.
Standard
Ratio-Balanced
Component Therapy
Outcomes
Measurements
Sampling

PPOWER

- Pragmatic, Prehospital, group O, Whole Blood Early Resuscitation trial

- Single site; EFIC- IND required- Obtained
- 3 yr prospective randomized pilot trial
- O-NEG LTLR-WB Prehospital
- O-POS LTLR-WB In Hospital
- N=112; 1 interim analysis
- Randomized- Helicopter base (4 bases)

PPOWER

INCLUSION

1. Blunt or penetrating injured patients at risk of hemorrhage being transported from scene or referral hospital to a participating PPOWER trial site

AND 2A. OR 2B.

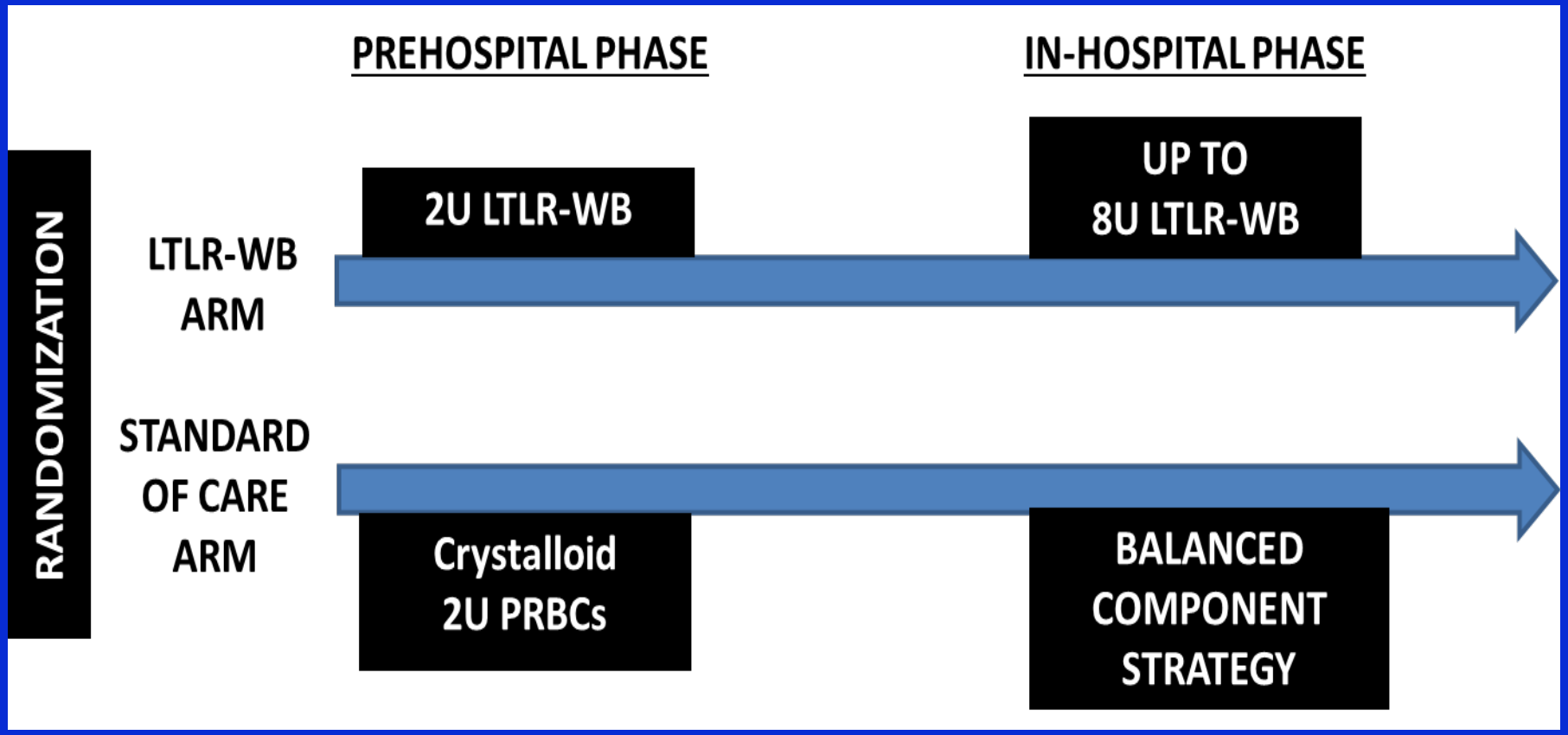
2A. Systolic blood pressure ≤ 90mmHg AND tachycardia >108 at scene, at outside hospital or during transport.

2B. Systolic blood pressure ≤ 70mmHg without tachycardia requirement, at scene, at outside hospital or during transport.

PPOWER

EXCLUSION

1. Documented Age ≥ 90 or < 18 years of age
2. Inability to obtain intravenous or interosseous access
3. Isolated fall from standing injury mechanism
4. Known prisoner or known pregnancy
5. Traumatic arrest with > 5 minutes of CPR without return of vital signs
6. Brain matter exposed or penetrating brain injury (GSW)
7. Isolated drowning or hanging victims
8. Isolated burns without evidence of traumatic injury
9. Referral hospital in-patient admission
10. Objection to study voiced by subject or family member at scene
11. Wearing NO PPOWER opt-out bracelet


PREHOSPITAL PHASE
IN-HOSPITAL PHASE
RANDOMIZATION
LTLR-WB ARM
2U LTLR-WB
UP TO 8U LTLR-WB
STANDARD OF CARE ARM
Crystalloid 2U PRBCs
BALANCED COMPONENT STRATEGY

PPOWER

Outcomes:

AIM 1: Feasibility-enrollment rate, eligibility, adherence, enrollment characteristics

AIM 2: Efficacy and Safety – 28 day mortality; acute hemolytic transfusion reaction

Secondary Outcomes- MOF, shock severity and correction, ARDS, NI, Mortality – 3,6 24 hrs, blood component transfusion requirements

AIM 3: Mechanistic drivers- TEG/PT/INR; Platelet activation, aggregation and adhesion; glycoalyx integrity; donor exposure, age and volume of transfusion products

FDA IND


GO TO
JAIL


Chance
GO DIRECTLY
TO JAIL
DO NOT PASS GO, DO NOT COLLECT $200

STOP

PPOWER EFIC

IRB

FDA

Community
Consultation

PPOWER

Challenges

- Gender / group O negative/positive
- Cluster design by base
- Safety and Efficacy outcome vs Feasibility

Begin Enrollment 2018

Questions

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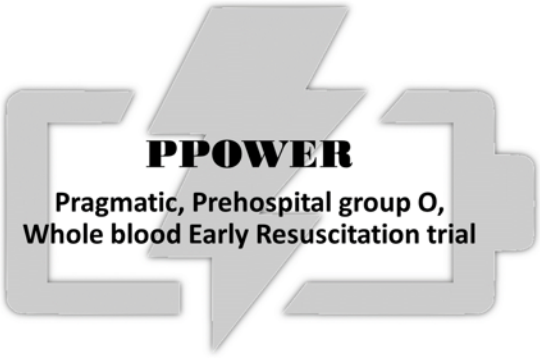
PPOWER
Pragmatic, Prehospital group O,
Whole blood Early Resuscitation trial


LiTES