We Don't Know How It Works, But It Works!

TRANscending a new EXAMination & understanding of an old ACID:

The Role of Tranexamic Acid in EMS

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EMS System for Metropolitan Oklahoma City & Tulsa
Professor & EMS Section Chief, Department of Emergency Medicine
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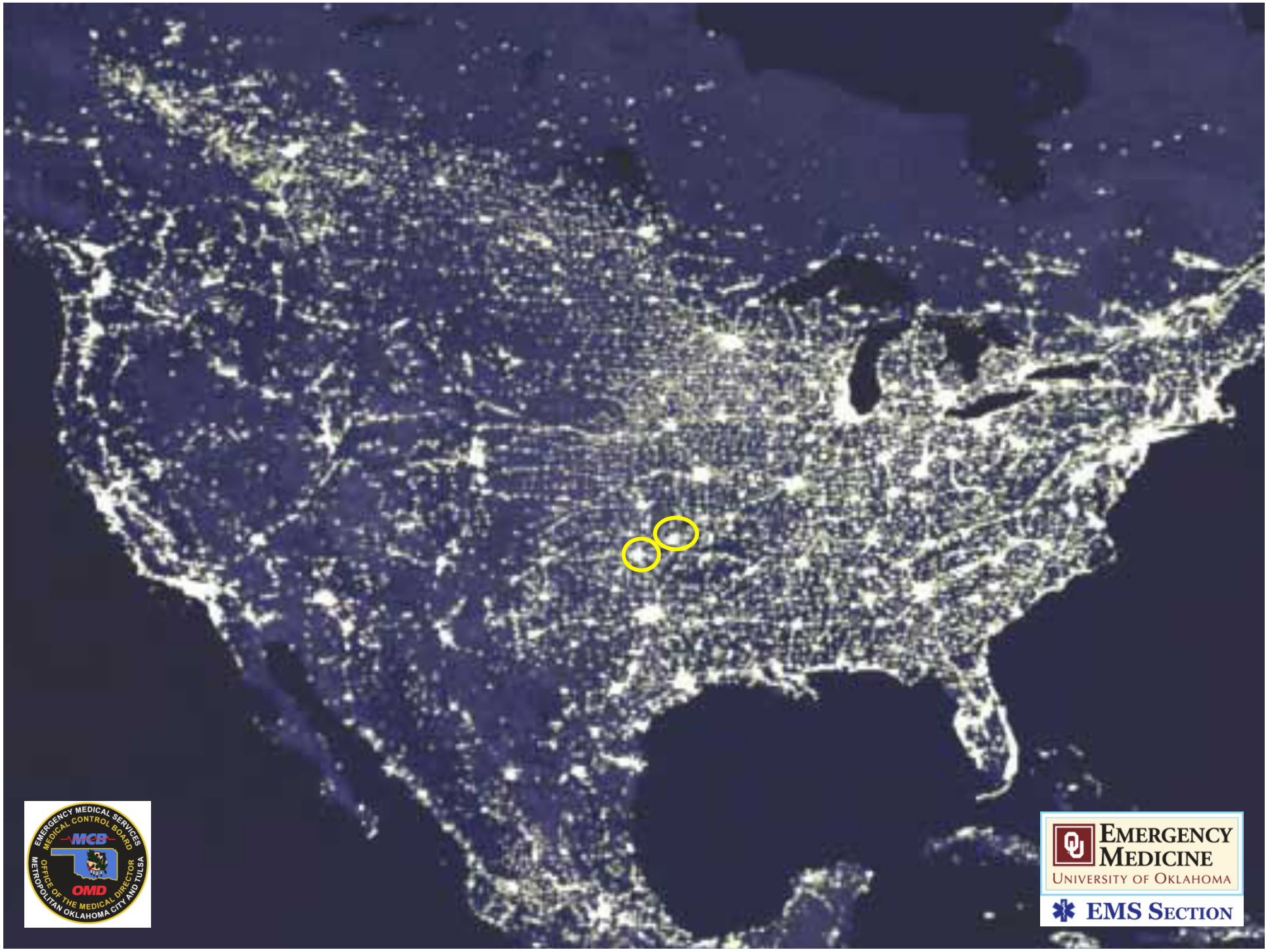
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EMS System for Metropolitan Oklahoma City &Tulsa

- 1,100 square miles
- Population
  - 1.6 million day
  - 1.2 million night
- 209,029 calls (2012)
- 142,467 transports (2012)
  - 68% transports

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Difference
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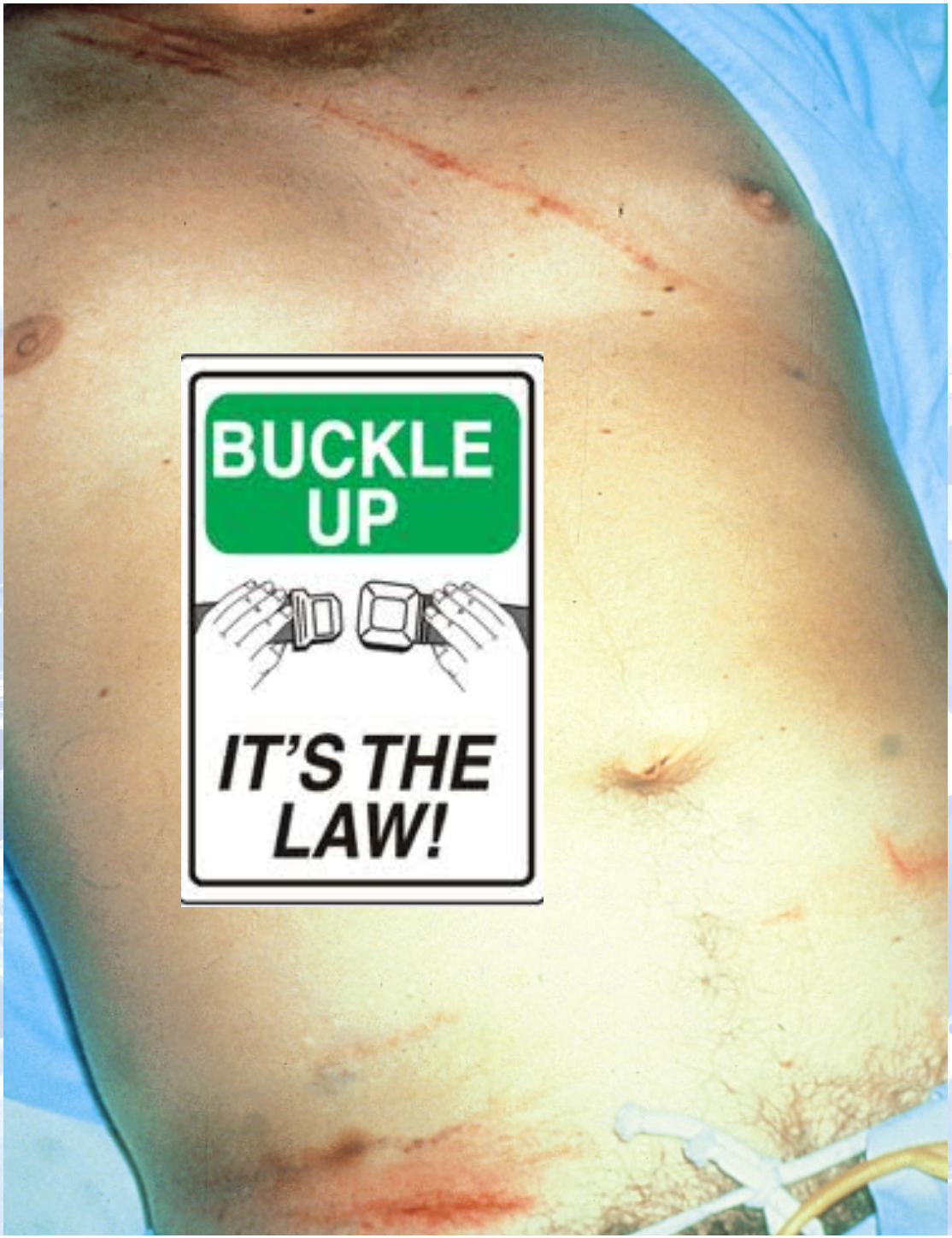

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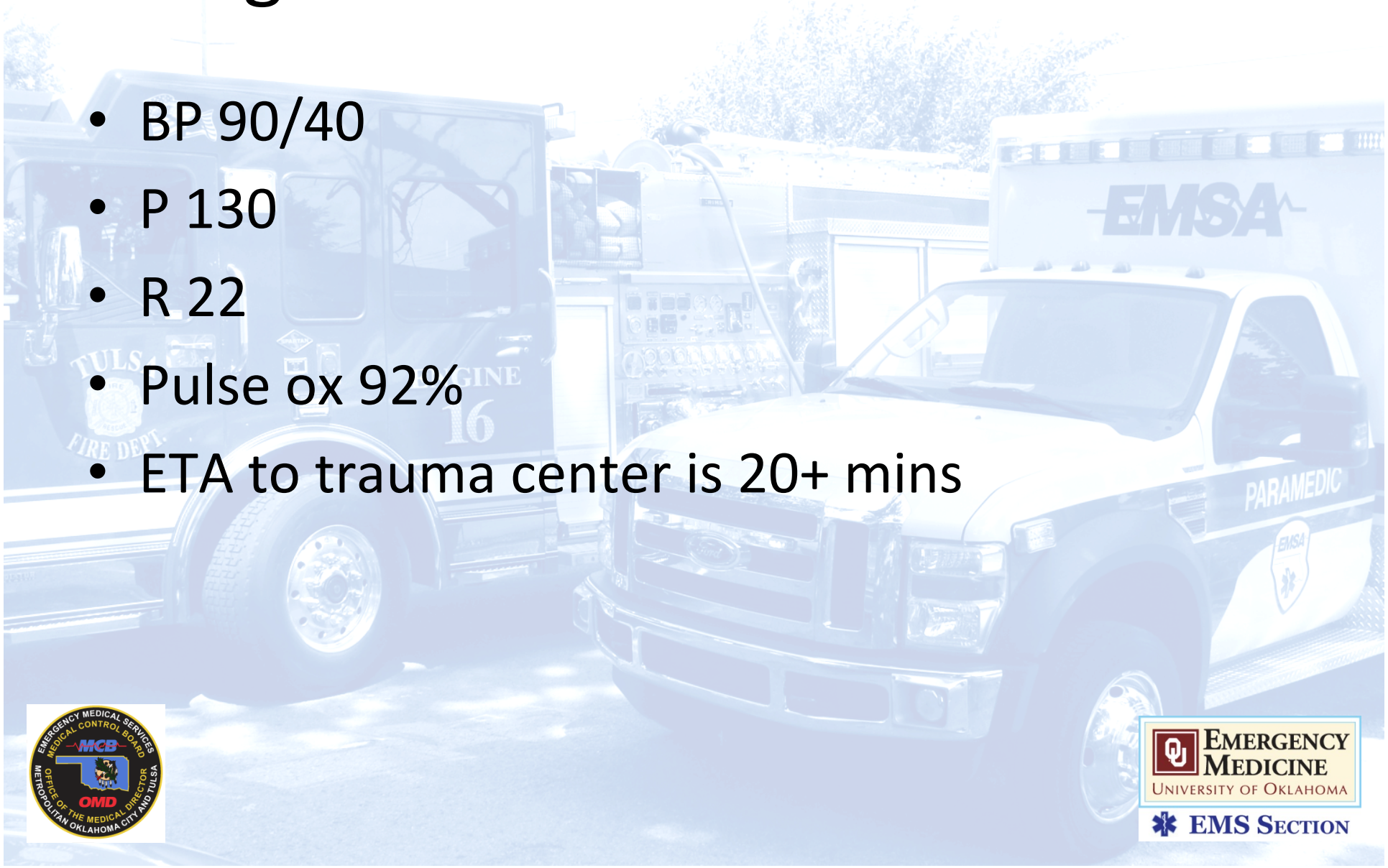
High-Force Abdominal Trauma

- BP 90/40
- P 130
- R 22
- Pulse ox 92%
- ETA to trauma center is 20+ mins



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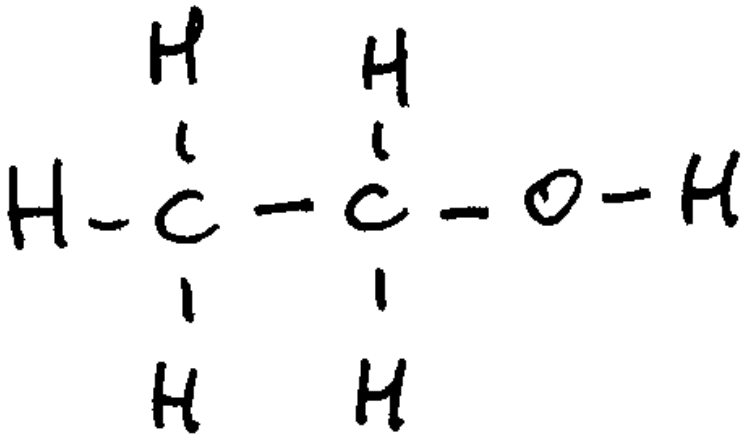

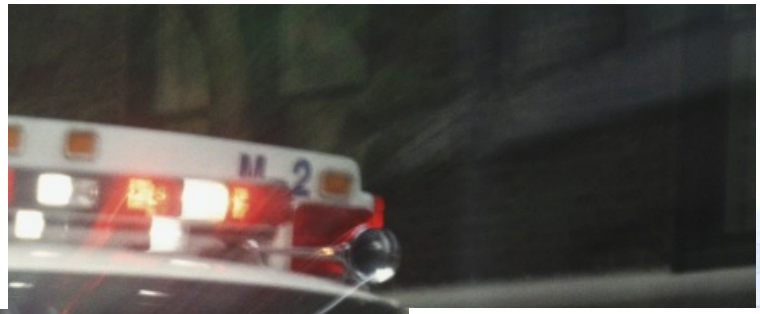

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Tranexamic Acid?

By EMS?

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What is TXA?

- Antifibrinolytic
- Anti – "Clot buster"
- Clot stabilizer (inhibits clot breakdown)
- Likely more…Anti-inflammatory modulator?

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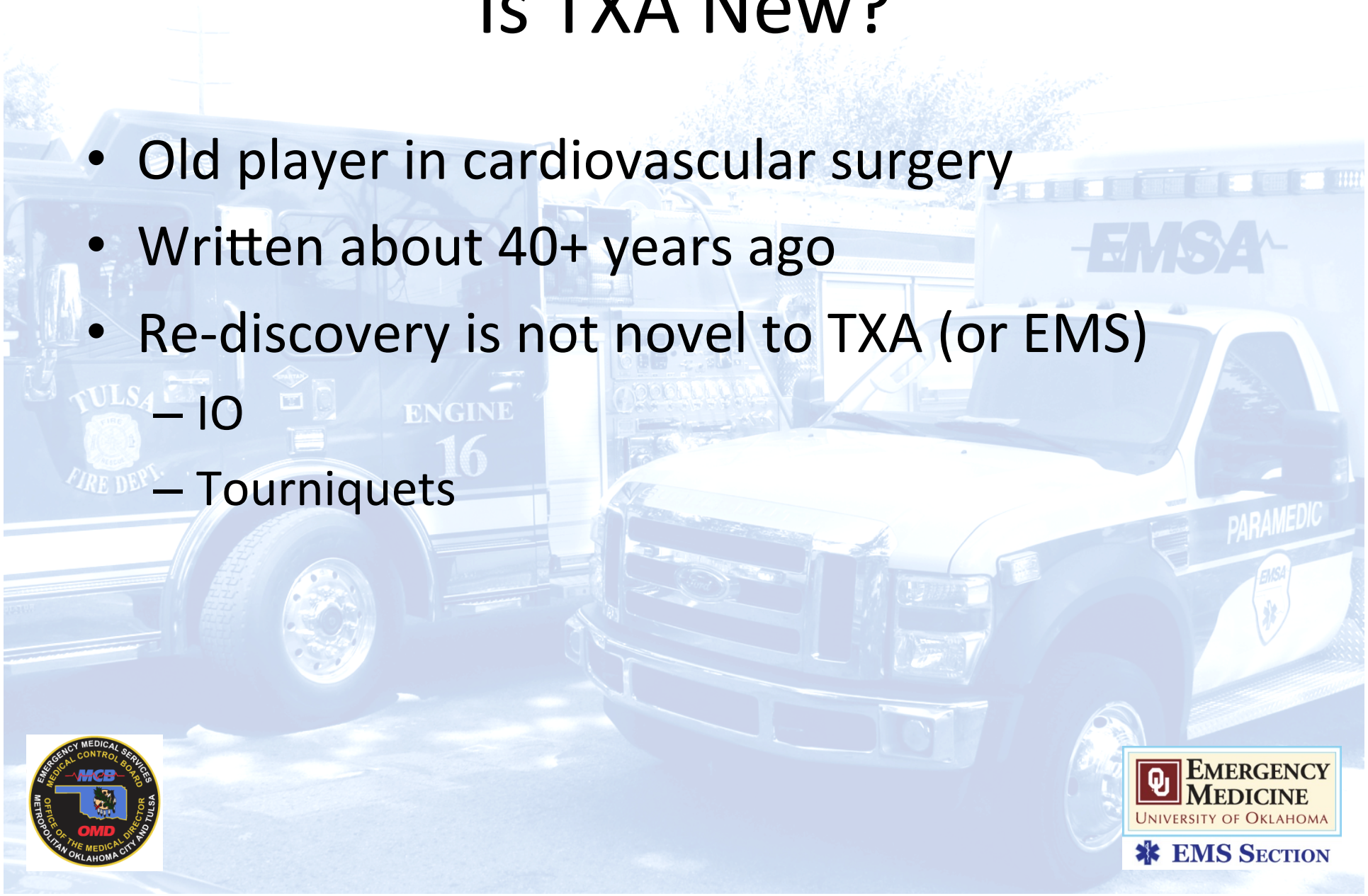
Is TXA New?

- Old player in cardiovascular surgery
- Written about 40+ years ago
- Re-discovery is not novel to TXA (or EMS)
  - IO
  - Tourniquets



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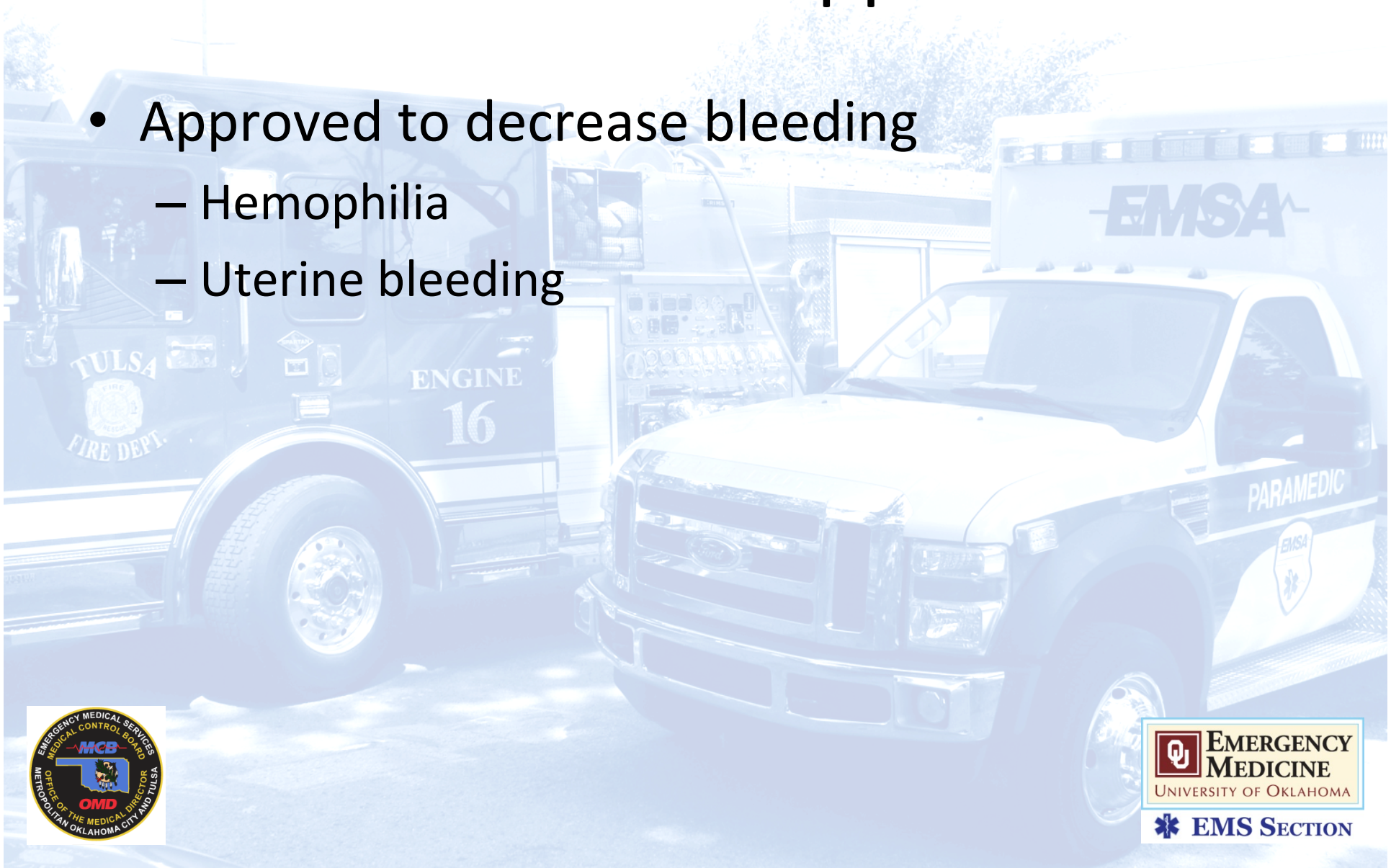
Does the FDA approve?

- Approved to decrease bleeding
  - Hemophilia
  - Uterine bleeding



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CRASH-2

Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage 2

Lancet. 2010 Jul 3;376(9734):23-32

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CRASH-2 Study Design

- Prospective civilian trauma patients
- Randomized controlled trial
- 274 hospitals in 40 countries
- 20,211 adult trauma patients
  - With, or risk of, significant bleeding
  - HR >110, SBP <90 mmHg, clinical judgment
- Treatment within 8 hours of injury
  - TXA or placebo

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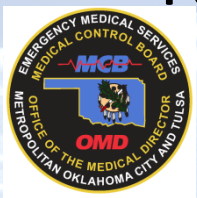
CRASH-2 Study Outcome Points

- Death in hospital within 4 weeks of injury
  - Bleeding
  - Vascular occlusion (MI, stroke, PE)
  - Multiorgan failure
  - Head injury
  - "Other"
- Vascular occlusive events
- Need for blood transfusion/surgery



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CRASH-2 Study Results

- All cause mortality (TXA)
  - 14.5% v 16.0%
  - RR 0.91
  - 95% CI 0.85 - 0.97
  - p = 0.0035
- Death due to bleeding (TXA)
  - 4.9% v 5.7%
  - RR 0.85
  - 95% CI 0.76 - 0.96
  - p = 0.0077

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CRASH-2 Study Results

NNT = 67

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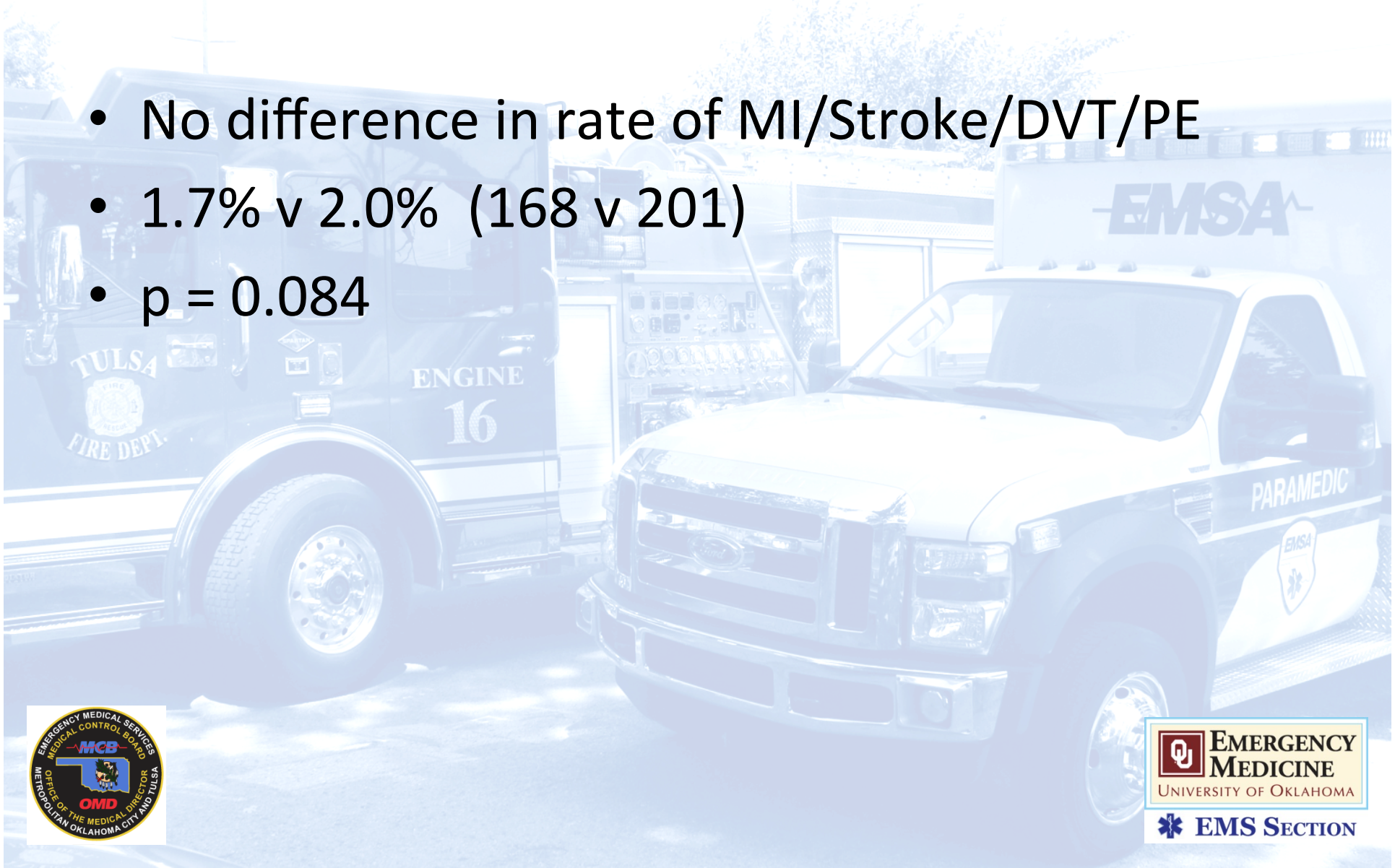
TXA – Is there harm?

- No difference in rate of MI/Stroke/DVT/PE
- 1.7% v 2.0% (168 v 201)
- p = 0.084



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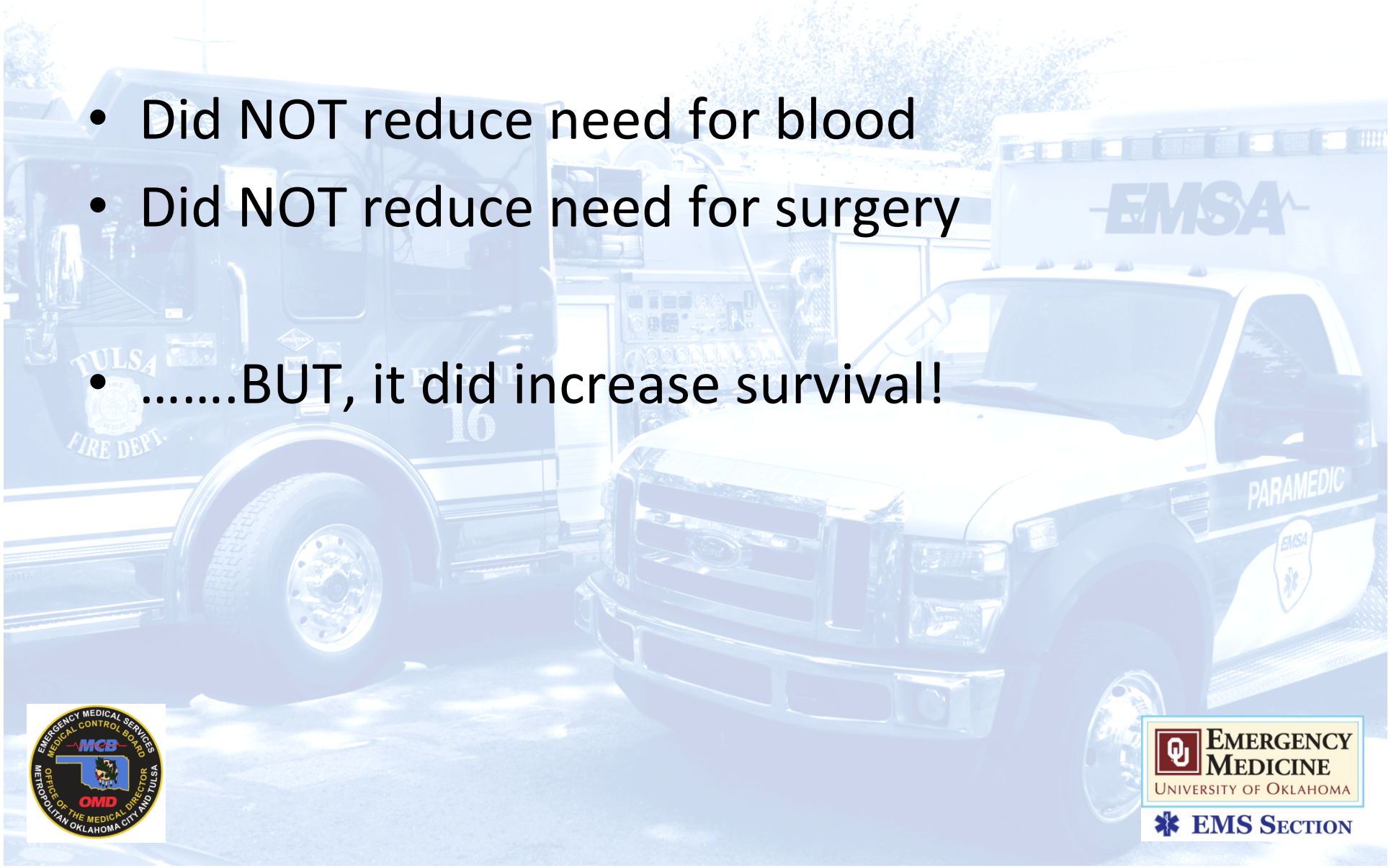
TXA – Treatment Course Effects?

- Did NOT reduce need for blood
- Did NOT reduce need for surgery

- …….BUT, it did increase survival!



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MATTERs

Military Application of Tranexamic Acid in Trauma Emergency Resuscitation Study

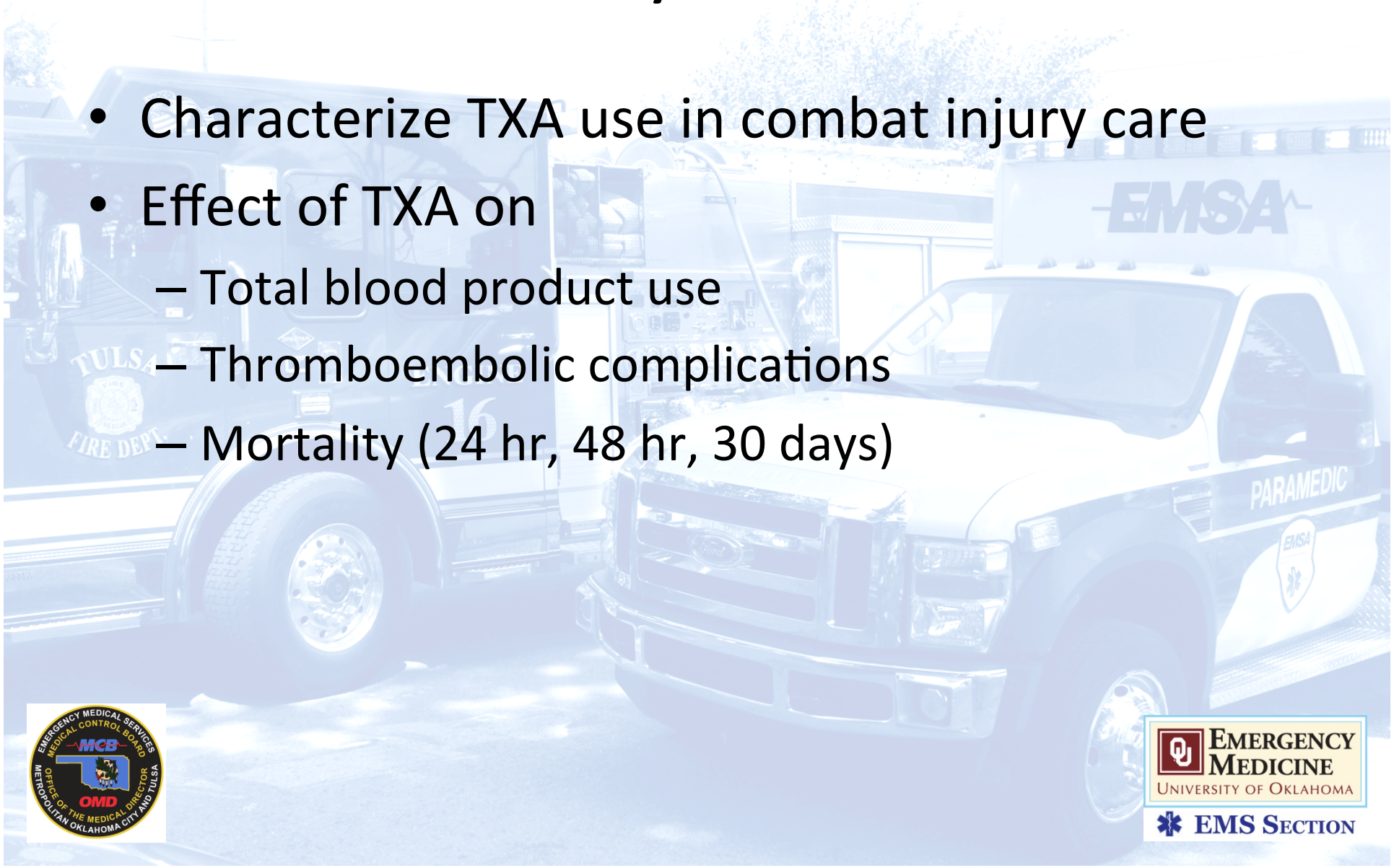
Arch Surg. 2012 Feb;147(2):113-9.

MATTERs Study Design

- Retrospective combat casualties
  - British helo physicians in Afghanistan
- TXA v no TXA if receiving 1+ uPRBC
  - Subgroup massive transfusion (10+)
- 896 consecutive admissions
  - 293 received TXA (IV bolus only)

MATTERs Study Outcome Points

- Characterize TXA use in combat injury care
- Effect of TXA on
  - Total blood product use
  - Thromboembolic complications
  - Mortality (24 hr, 48 hr, 30 days)



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MATTERs Study Results

- TXA lower mortality - overall
  - 17.4% v 23.9% (p = 0.03)
  - Mean ISS higher in TXA group (25.2 v 22.5; p<0.001)
- TXA lower mortality – massive transfusion
  - 14.4% v 28.1% (p = 0.004)
  - Survival odds ratio 7.228 (95% CI 3.0 – 17.3)

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MATTERs Study Results

NNT = 7

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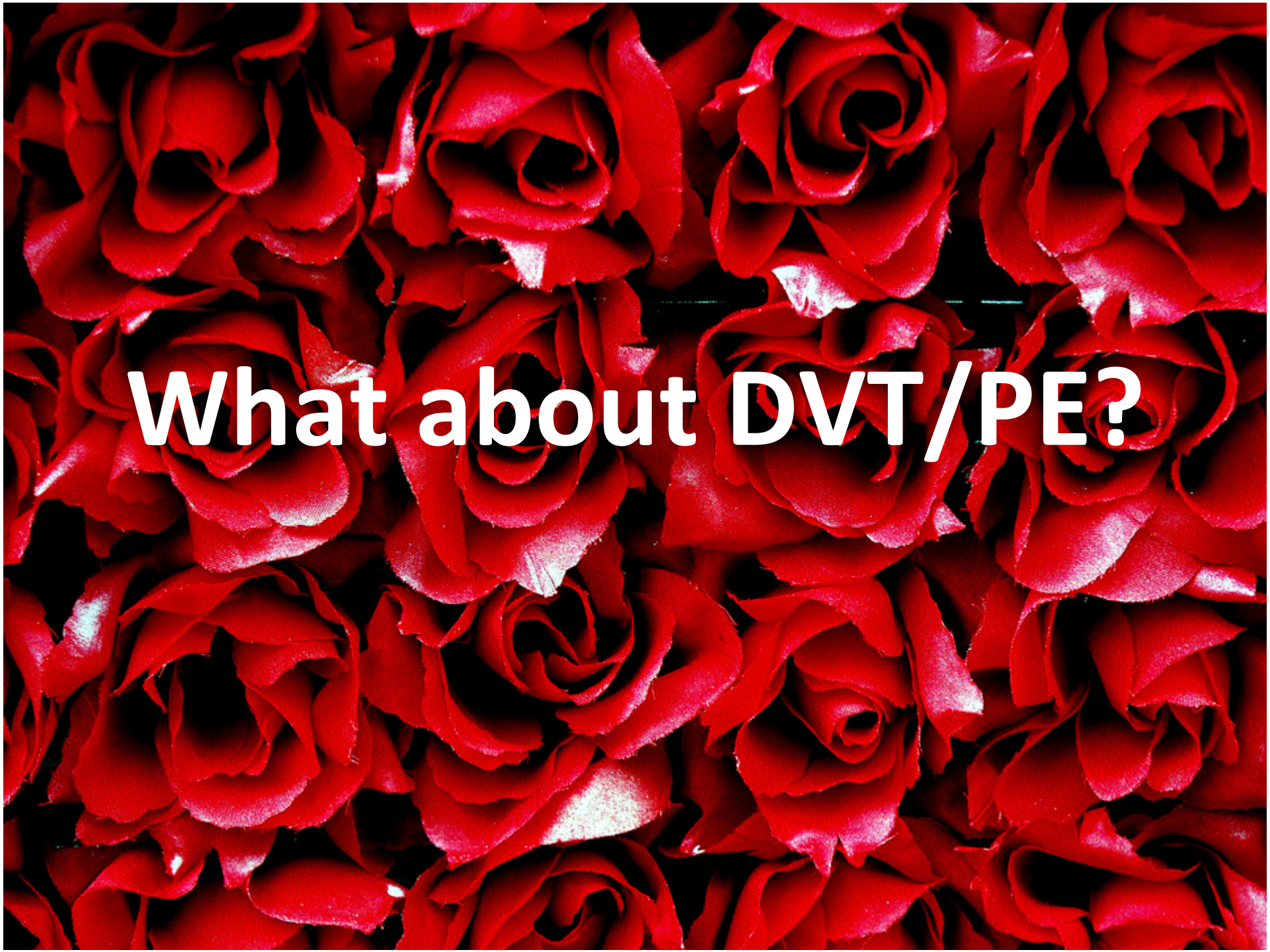
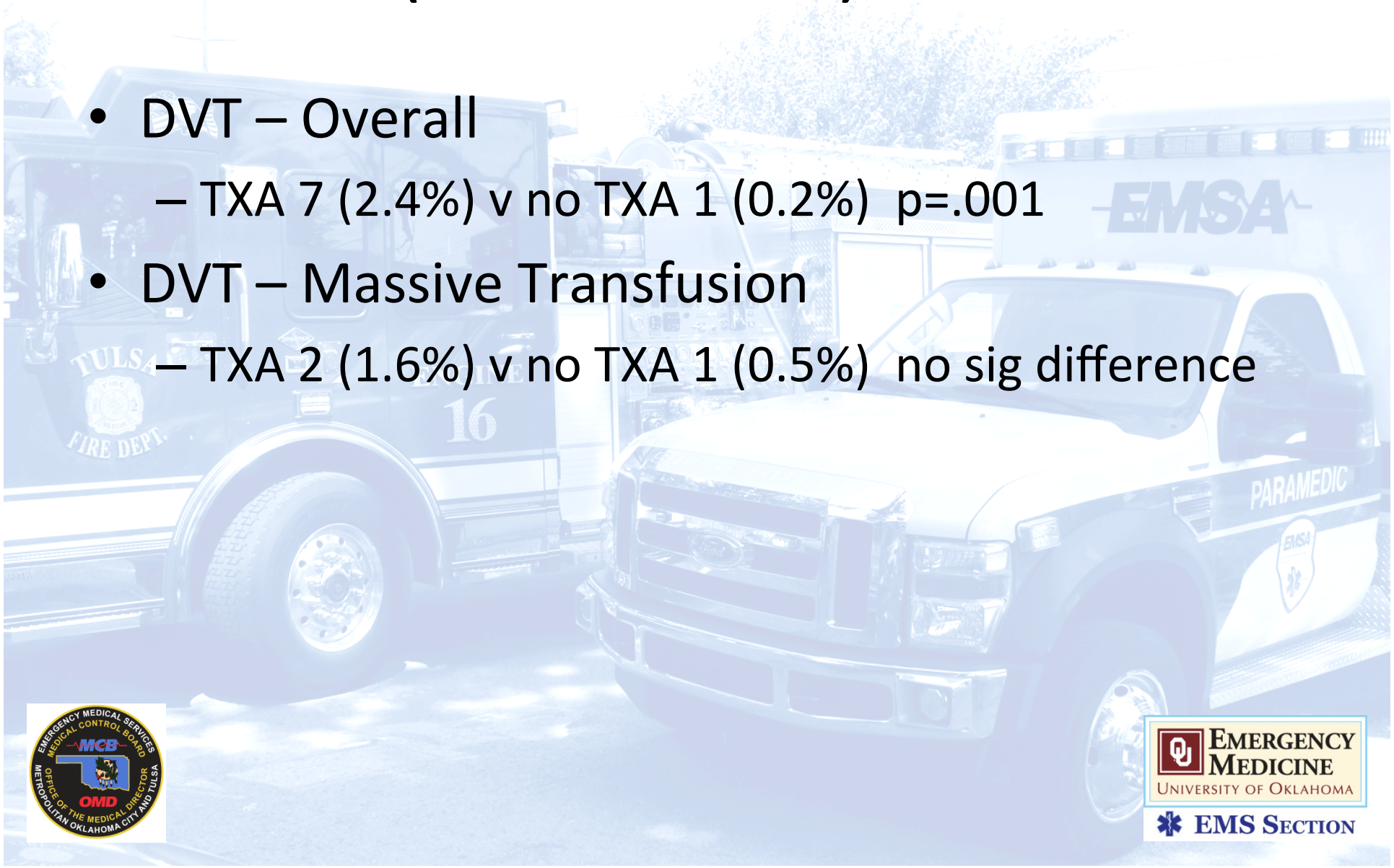

What about DVT/PE?

Matters (of Concern?) in MATTERs

- DVT – Overall
  - TXA 7 (2.4%) v no TXA 1 (0.2%) p=.001
- DVT – Massive Transfusion
  - TXA 2 (1.6%) v no TXA 1 (0.5%) no sig difference



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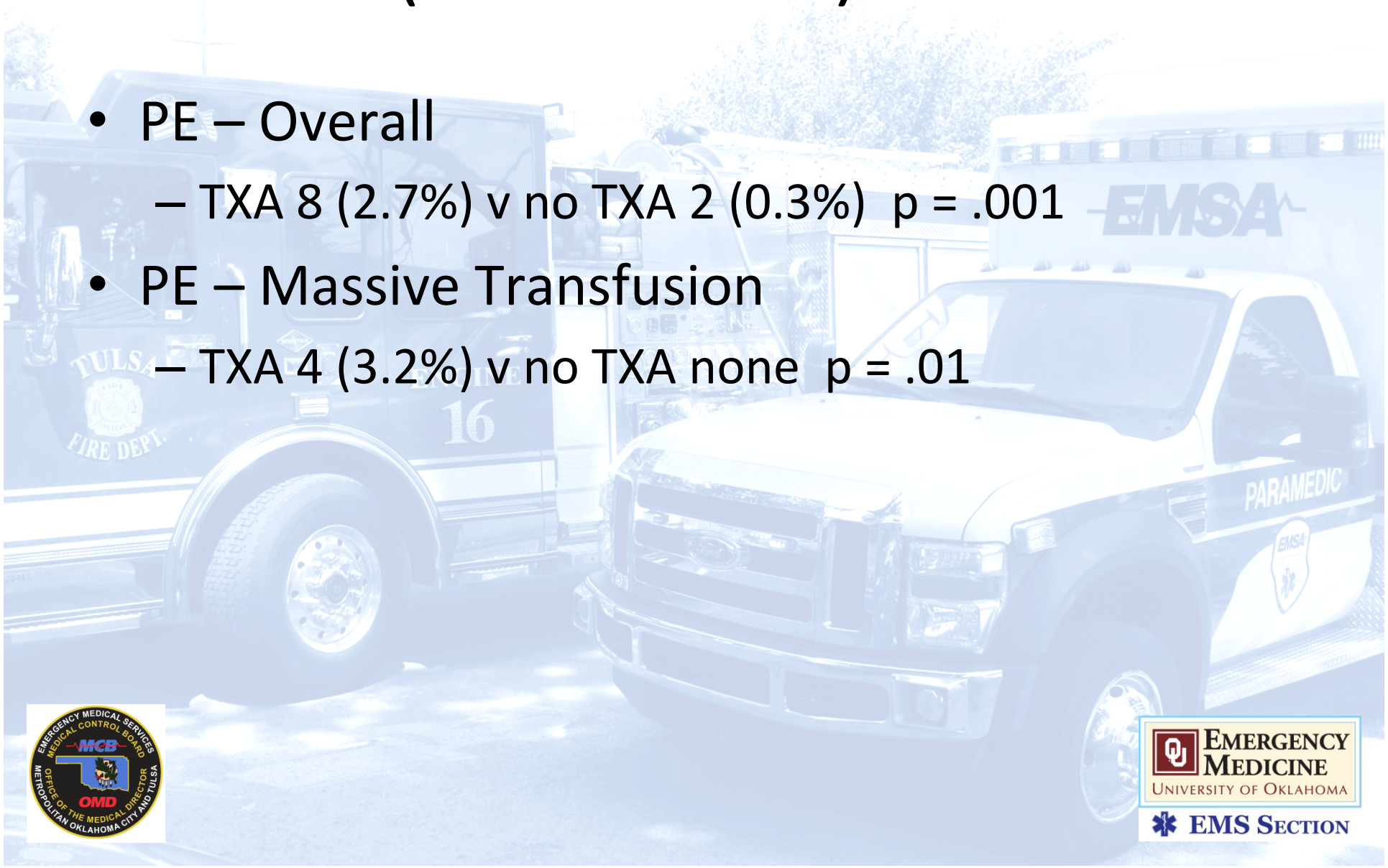
Matters (of Concern?) in MATTERs

- PE – Overall
  - TXA 8 (2.7%) v no TXA 2 (0.3%) p = .001
- PE – Massive Transfusion
  - TXA 4 (3.2%) v no TXA none p = .01



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MATTERs TXA Group

- Higher injury burden = More thrombotic event
- ? Military theater – penetrating/ortho
- ? Survival allows for DVT/PE to be diagnosed
- ? Retrospective design limitations
  - Screening/diagnostic approaches
  - DVT/PE clinical significance

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MATTERS Take-Aways

- Survival benefit to any patient getting blood
- Massive transfusion? (10u PRBC + / 24 hrs)
  - TXA independent predictor of survival
- Benefit not really shown until 48 hrs
  - Can't be clot function alone
  - ? Anti-inflammatory component
- Earlier the better….as in first hour post trauma

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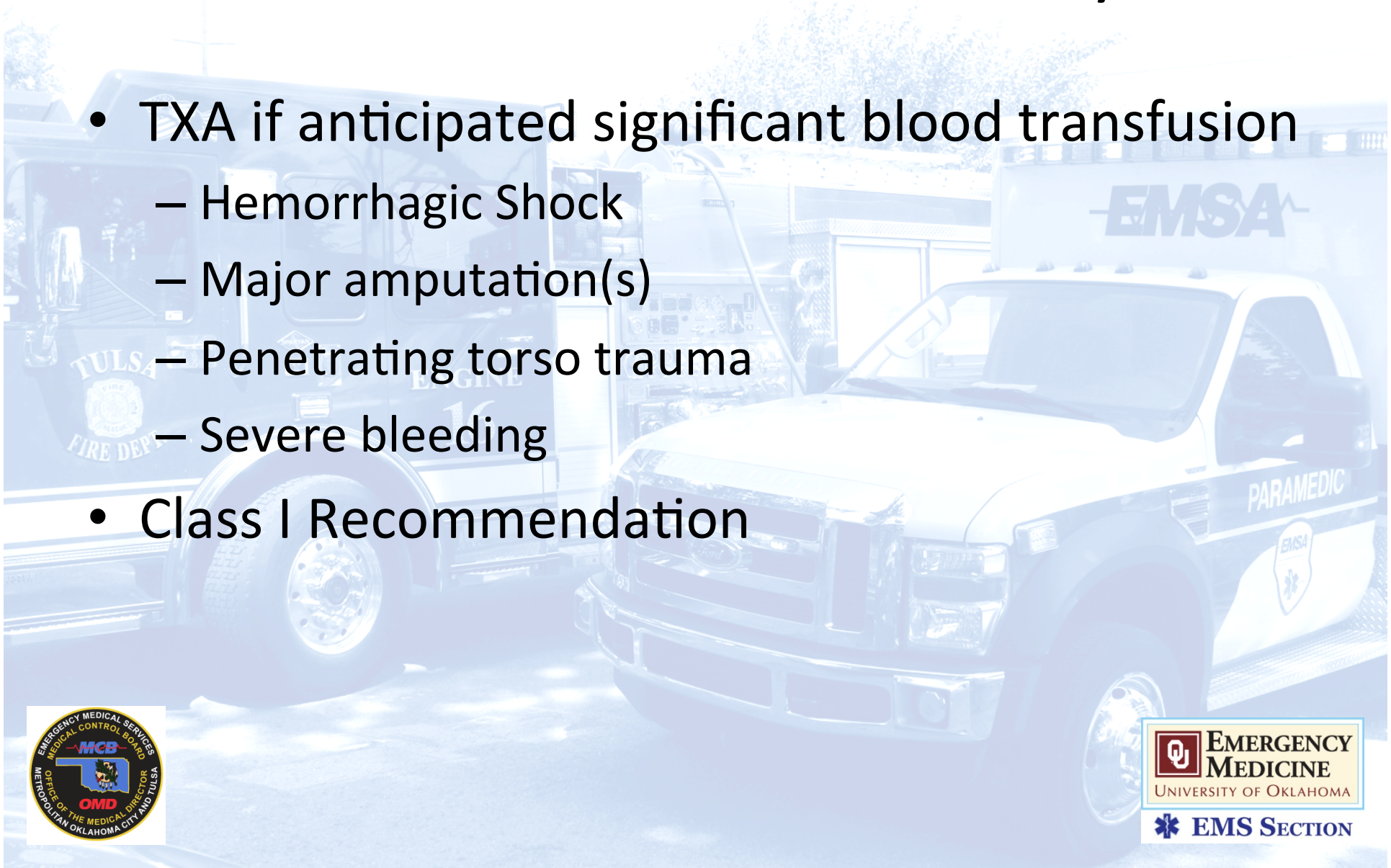
TCCC = Tactical Combat Casualty Care

- TXA if anticipated significant blood transfusion
  - Hemorrhagic Shock
  - Major amputation(s)
  - Penetrating torso trauma
  - Severe bleeding
- Class I Recommendation



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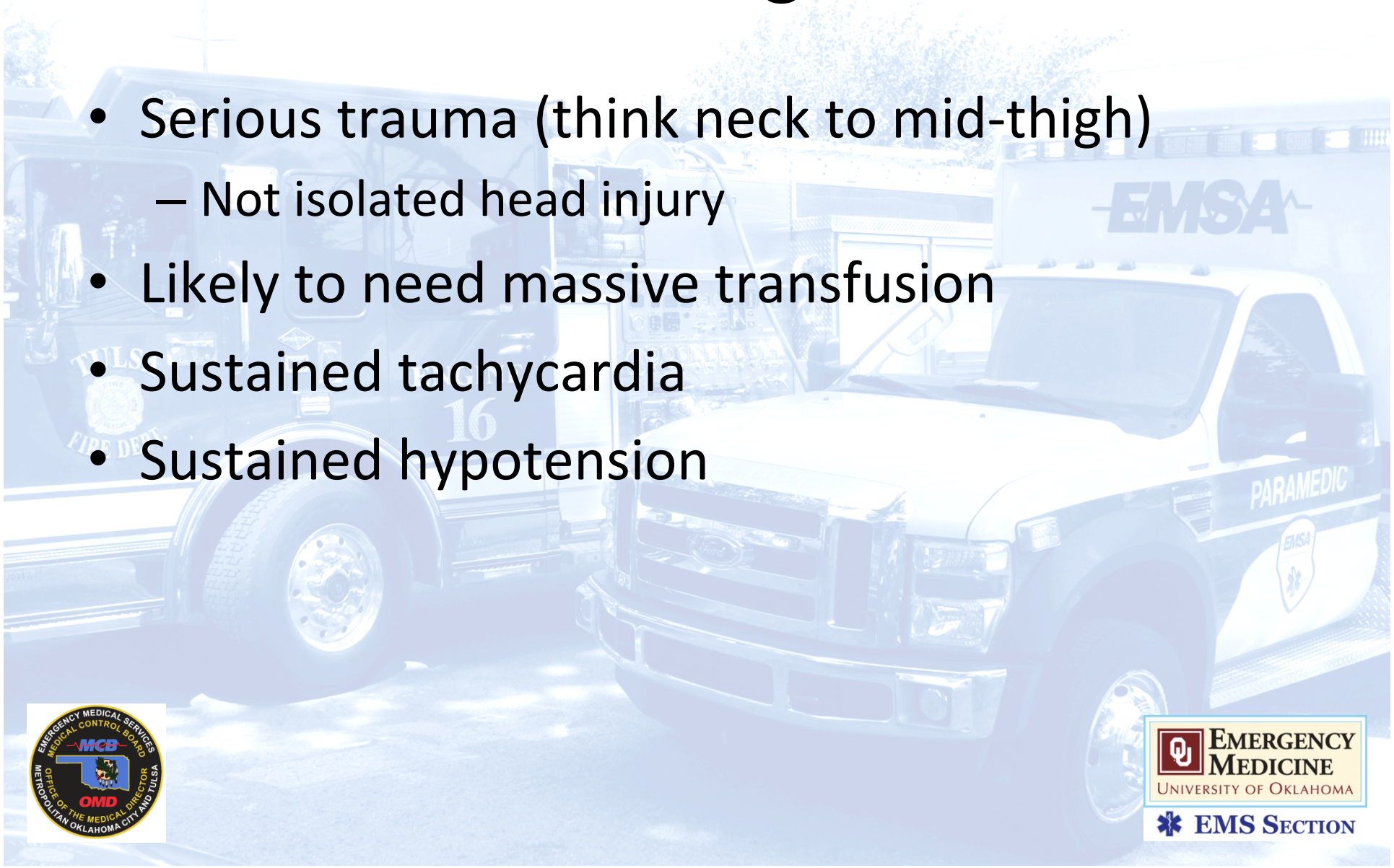
Who should get TXA?

- Serious trauma (think neck to mid-thigh)
  - Not isolated head injury
- Likely to need massive transfusion
- Sustained tachycardia
- Sustained hypotension



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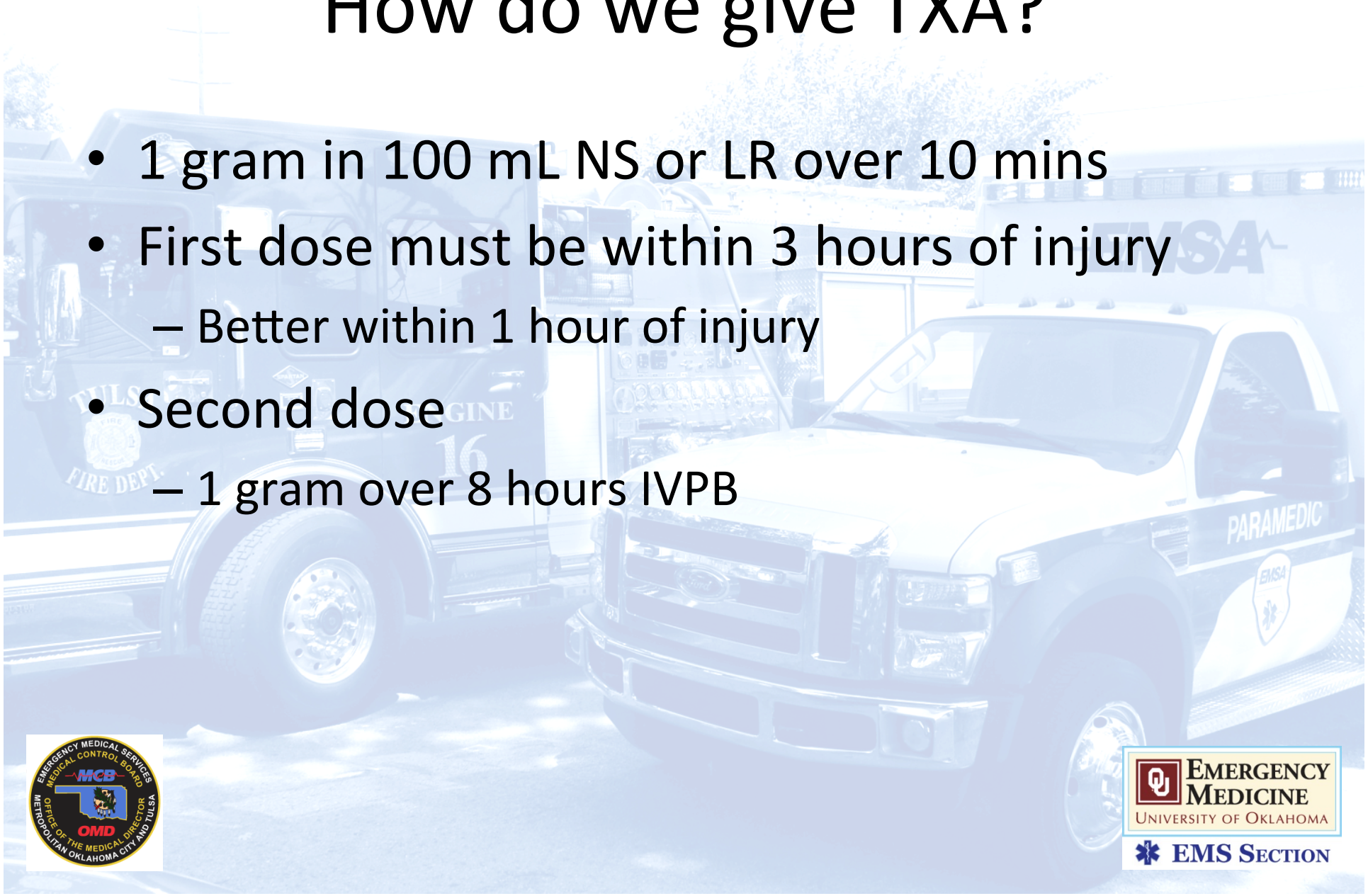
How do we give TXA?

- 1 gram in 100 mL NS or LR over 10 mins
- First dose must be within 3 hours of injury
  - Better within 1 hour of injury
- Second dose
  - 1 gram over 8 hours IVPB



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What does TXA cost?

- Military $1.50 a dose ($10 - 100/life)
- Civilian $55 a dose ($385 – 3,685/life)

- Military considers shelf life in years
- Manufacturer likely doesn't
- Advised temps 59-86 degrees F
- Viewed very heat stable in Middle East

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TXA – Where do we go?

- "Early adopters"
  - OKC & TUL effective 4/1/13 (est. 60+ pts/year)
  - London Ambulance Service 4/1/13
- Ongoing study - ?DVT/PE risk
  - No evidence in CRASH-2
  - Mostly transfusion ratios + TXA
- Likely won't see scope of CRASH-2 again

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Take Home Points

- No current EMS answer for all bleeding
- Should EMS administer TXA?
  - Good clinical benefit shown in EBM
  - Must administer early (within 3 hrs of injury)
  - Good safety profile (vasoocclusive events)
  - Fits in operational/fiscal realities
- Discussion with trauma surgeons essential

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Protocol Resources

okctulomd.com

"Training & Protocols" tab

MCB Pre-Hospital Operational Standards

2013 State of Oklahoma EMS Protocols
Field & Reference Editions

TULSA FIRE DEPARTMENT
PROTECTING LIFE, HEALTH, PROPERTY & ENVIRONMENT
EST. 1900

OKC FIRE • RESCUE • EMS
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