The Trauma Survivors Outcomes & Support (TSOS) Trial as an ePCT Training Case Study

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Overview: TSOS as an ePCT Case Study

- NIH Collaboratory ePCT training themes relevant to TSOS
NIH Collaboratory ePCT Training Workshop:  
Key Themes for TSOS

• Two day workshop: Feb 20-21, 2018  
• NIH Collaboratory faculty  
• Key Themes relevant to TSOS  
  - PRECIS-2 as a pragmatic trial descriptor  
  - Pragmatic trials target a clinical decision  
  - Follow-up endpoints in ePCTs  
  - Tradeoffs inevitable in pragmatic trials  
  - Pragmatic trial regulatory complexity  
  - Choice of cluster randomized design
Overview: TSOS as an ePCT Case Study

- TSOS PRECIS-2 Wheel
- TSOS historical development & update
- TSOS policy decision target
- TSOS & follow-up intensity
- TSOS regulatory complexity
- Cluster randomized design choices
TSOS as an ePCT Training Case Study
**PRECIS-2 Wheel**

- **Eligibility**: Who is selected to participate in the trial?
- **Recruitment**: How are participants recruited into the trial?
- **Setting**: Where is the trial being done?
- **Organisation**: What expertise and resources are needed to deliver the intervention?
- **Flexibility: adherence**: What measures are in place to make sure participants adhere to the intervention?
- **Flexibility: delivery**: How should the intervention be delivered?
- **Primary outcome**: How relevant is it to participants?
- **Follow-up**: How closely are participants followed-up?
- **Primary analysis**: To what extent are all data included?

TSOS PRECIS-2 Wheel
TSOS Study Design

- 25 US trauma centers
- Stepped wedge cluster randomization
- All sites begin recruiting controls
- Intervention “turned on” at each site
- 40 patients per/site goal (960 pts. total)
- Patients provide informed consent
- Baseline PTSD & comorbidity assessment
- 3, 6 and 12 month follow-up interviews
TSOS PRECIS-2 Wheel

- Eligibility
- Recruitment
- Setting
- Organization
- Flexibility Delivery
- Flexibility Adherence
- Follow-Up
- Primary Outcome
- Primary Analysis
TSOS Pragmatic Trial Update

- 25 US level I trauma center sites
- 935 Patients consented/screened
- 62.5% PTSD EHR screen in rate
- 585 patients randomized
  - 372 Control
  - 213 Intervention
- Stepped wedge intervention roll-out
  - 4/4 intervention waves trained
- 75-80% 3 & 6 mo. follow-up to date
- 70-75% 12 month follow-up
TSOS Hypotheses & Aims

• The intervention group when compared to the control group will demonstrate:
  1) ↓ PTSD symptoms (primary hypothesis)
  2) ↓ Depressive symptoms
  3) ↓ Suicidal ideation
  4) ↓ Alcohol use problems
  5) Improved post-injury physical function

• Regulatory policy collaboration with American College of Surgeons Committee on Trauma
TSOS Designed to Impact American College of Surgeons Policy Decisions
Historical Development: TSOS Policy Target

Two decades of orchestrated clinical trials & American College of Surgeons policy partnership builds practice change momentum into ePCT design & implementation
“Alcohol is such a significant associated factor and contributor to injury that it is vital that level I and level II trauma centers have a mechanism to identify patients who are problem drinkers.”

“In addition, level I centers must have the capability to provide an intervention for patients identified as problem drinkers.”
SBIRT in Emergency Care Settings: Are We Ready to Take it to Scale?

Edward Bernstein, MD, Judith A. Bernstein, RNC, PhD, Jack B. Stein, PhD, and Richard Saitz, MD, MPH

Abstract

This article summarizes a panel discussion on “SBIRT in the emergency care setting: are we ready to take it to scale?” Dr. Edward Bernstein commented on the historical developments of emergency department (ED) screening, brief intervention (BI), and referral to treatment (SBIRT) research, practice, and knowledge translation. Dr. Jack Stein addressed SBIRT grant program progress to date, the reimbursement stream, SBIRT lessons learned, and unanswered questions. Dr. Richard Saitz reviewed the limitations of the evidence for alcohol and drug ED screening and BI and cautioned on the danger of proceeding to practice and broad dissemination without evidenced based on randomized controlled trials with sufficient sample size and clinically important outcomes.

Disseminating Organizational Screening & Brief Interventions (DO-SBIS)

Evidence-based Interventions for Alcohol Problems in Trauma Centers
TSOS Pragmatic Trial Progenitor: Disseminating Organizational Screening and Brief Intervention Services (DO-SBIS)

- Targets alcohol screening and intervention
- 20 US Level I Trauma Centers
- 878 patients receive baseline EHR screen
- 6 & 12 month follow-up interviews
- Parallel Group Cluster Randomized
- University of Washington IRB “Coordinates”
  - 20 site IRBs
  - Consent documents retained at sites
  - Study appointed DSMB familiar with “real world” alcohol effectiveness trials
DO-SBIS Results: All Patients (N = 878)

% at Risk Drinking (AUDIT)

- Intervention
- Usual Care

Baseline | 6 | 12
---|---|---

$\rho < 0.05$
Alcohol Universal Screening & Intervention at Level I & II trauma centers
TSOS Designed to Impact American College of Surgeons Policy

• TSOS design builds from DO-SBIS
PTSD screening & intervention best practice guideline recommendation
Follow-up Endpoints in ePCTs: TSOS as a Case Study
Choosing an endpoint that is not captured reliably as part of routine clinical care is not pragmatic.
PRECIS-2 Wheel

Eligibility
Who is selected to participate in the trial?

Recruitment
How are participants recruited into the trial?

Setting
Where is the trial being done?

Organisation
What expertise and resources are needed to deliver the intervention?

Flexibility: adherence
What measures are in place to make sure participants adhere to the intervention?

Flexibility: delivery
How should the intervention be delivered?

Primary analysis
To what extent are all data included?

Primary outcome
How relevant is it to participants?

Follow-up
How closely are participants followed-up?

TSOS PRECIS-2 wheel

Primary Analysis

Primary Outcome

Follow-Up

Eligibility

Recruitment

Setting

Organization

Flexibility Adherence

Flexibility Delivery
TSOS Study Design

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Care Transition Pragmatic Trial Follow-up Beyond Routine Visits: Comprehensive Post-Acute Stroke Services Study (COMPASS, P Duncan PI)

- PCORI pragmatic trial
- Stroke survivors in acute care hospitals in a single state
- Primary outcome: PROs
  - Stroke impact scale PRO post-discharge
  - Readmissions and mortality also tracked but unavailable in population level administrative database
Towards Population Level Administrative Data for Pragmatic Trial Care Transition Interventions: Emergency Department Information Exchanges (EDIE)

- Washington & Oregon State
- Population level ED data
- Accrues on Intent-to-treat sample
- No additional clinical follow-up required
Single Site Care Transition Pragmatic Trial Data Using EDIE: Intervention Reduces Statewide Emergency Department Utilization

FIGURE 2. Intervention and control group emergency department visits over the course of the 12 months after injury. Note. N = 171 at all time points; ED = emergency department; m = months.
TSOS Regulatory Complexity
DO-SBIS Successful Implementation Informs TSOS Regulatory Approach

• UW Coordinating IRB & 20 site IRBs
• DSMB and IRB communication
• Pragmatic approach gives sites relative regulatory autonomy
• In DO-SBIS study informed consent is obtained and documentation retained at sites
TSOS Regulatory Complexity

• WIRB as centralized IRB
• 21/25 sites elect not to use WIRB
• Pragmatic approach gives sites relative regulatory autonomy
• As in DO-SBIS study informed consent is obtained and documentation retained at sites
TSOS PRECIS-2 wheel
TSOS Pragmatic Trial Regulatory Tension: Generalizable Sites vs. Regulatory Expertise

• One site undergoes internal audit
• One site undergoes voluntary recruitment suspension by TSOS team
• One site cannot account for consented patient: Consent form review begins
• Review reveals a site with major informed consent procedure difficulties
• Recruitment at all sites temporarily suspended by DSMB
TSOS Movement Towards Increasingly Intensive Site Regulatory Monitoring

- Dedicated regulatory coordinator
- Prospective review of all informed consent documentation
- Reworking of recruitment workflow to include informed consent transfer to coordinating center
Choice of Cluster Randomized Design
Stepped Wedge Design

- Sites recruit control & intervention
- 25 sites randomized to 4 waves
- Begin with control recruitment
- Turn on intervention midway
Stepped Wedge Cluster Randomized Trial Design and Timeline

Unexposed to intervention (n=480 patients)

Exposed to intervention (n=480 patients)

Follow-up period

Accrual period

n=8
n=32

n=16
n=24

n=24
n=16

n=32
n=8

Year 1
July 2014
Jan. 1 2016
Year 2
July 2015
Year 3
July 2016
Year 4
July 2017
Year 5
July 2018

Q1   Q2   Q3   Q4      Q1  Q2     Q3  Q4       Q1  Q2      Q3   Q4         Q1    Q2    Q3    Q4         Q1   Q2   Q3    Q4

6 trauma centers/wave
Stepped Wedge Advantages

• All sites want and receive training
• Site variability in key factors mitigated as sites contribute patients to both control and intervention conditions
Stepped Wedge Disadvantages

- Control & intervention recruitment phased
- Phased roll-out limits trial flexibility particularly with regard to recruitment pauses
Summary
Summary: TSOS as an ePCT Training Case Study

• **Strengths**
  - Real world decision targeted
  - Generalizable sites, pts, providers

• **Weaknesses**
  - Ongoing development of pragmatic follow-up assessments
  - Regulatory intensity tradeoffs with site generalizability