The Trauma Survivors Outcome & Support (TSOS) Pragmatic Trial: Revisiting Effectiveness & Implementation Aims

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TSOS Outline

• Progress: Effectiveness aims
  - 635 patients recruited and randomized
  - Baseline data cleaning and analyses
  - Follow-up ongoing with 75-80% retention

• Progress: Implementation aims
  - Review of TSOS PRECIS-2 Wheel
  - Pragmatic methods for understanding trial implementation processes (RAPICE)
  - Initial Implementation process findings and implications for TSOS PRECIS-2 Wheel
TSOS Aims

1) Conduct pragmatic trial to determine intervention effectiveness – hypotheses are the intervention will:
   A) ↓ PTSD symptoms (PTSD Checklist)
   B) ↓ Depressive symptoms (PHQ-9)
   C) ↓ Alcohol use problems (AUDIT)
   D) ↑ Physical function (SF-12 PCS)

2) Understand trial implementation

3) Dissemination of results through American College of Surgeons’ policy
TSOS Progress Effectiveness Aims: Baseline Data Cleaning and Analyses
TSOS Study Design

- Cluster randomized stepped wedge design
- 25 US trauma centers
- EHR PTSD screen
- Baseline PTSD & comorbidity assessment
- All sites begin recruiting controls
- Intervention “turned on” at each site
TSOS Stepped Wedge Cluster Randomized Design

Patients Unexposed to intervention

Patients Exposed to intervention

Follow-up Period

Accrual period

Wave 1
n=8
n=32

Wave 2
n=16
n=24

Wave 3
n=24
n=16

Wave 4
n=32
n=8

6 centers/wave

Period 0
Period 1
Period 2
Period 3
Period 4

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

Yr 1 Yr 2 Yr 3 Yr 4 Yr 5
Results: TSOS Patient Flow

1064 Consented
\[\rightarrow\]
37 Did not complete PTSD Checklist
1027 PTSD Checklist Completed
\[\rightarrow\]
380 PTSD Checklist < 35
647 Screened In
\[\rightarrow\]
12 Excluded/Withdrawn
635 Randomized
370 Control
265 Intervention
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control (n=370)</th>
<th>Intervention (n=265)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>43%</td>
<td>55%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Non-White</td>
<td>54%</td>
<td>50%</td>
<td>ns</td>
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<tr>
<td>Intentional injury</td>
<td>38%</td>
<td>36%</td>
<td>ns</td>
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<tr>
<td>ICU Admit</td>
<td>62%</td>
<td>56%</td>
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<tr>
<td>Prior PTSD DX</td>
<td>15%</td>
<td>23%</td>
<td>&lt; 0.05</td>
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<tr>
<td>Prior Psych DX</td>
<td>40%</td>
<td>38%</td>
<td>ns</td>
</tr>
<tr>
<td>Prior antidepressant</td>
<td>21%</td>
<td>18%</td>
<td>ns</td>
</tr>
<tr>
<td>Prior opioids</td>
<td>11%</td>
<td>11%</td>
<td>ns</td>
</tr>
<tr>
<td>Age</td>
<td>40 yrs</td>
<td>38 yrs</td>
<td>&lt; 0.05</td>
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</table>
## TSOS Baseline Control vs. Intervention (N=635)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control (n=370)</th>
<th>Intervention (n=265)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>PTSD Checklist</td>
<td>50.7</td>
<td>54.0</td>
<td>&lt; 0.01</td>
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<tr>
<td>PHQ-9 Depression</td>
<td>13.9</td>
<td>14.3</td>
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<tr>
<td>PHQ-9 Item 9 Suicide+</td>
<td>24%</td>
<td>25%</td>
<td>ns</td>
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<tr>
<td>AUDIT Alcohol use</td>
<td>7.4</td>
<td>7.2</td>
<td>ns</td>
</tr>
<tr>
<td>SF-12 Phys. Function</td>
<td>49.1</td>
<td>49.7</td>
<td>ns</td>
</tr>
</tbody>
</table>
TSOS Follow-up Interview Status

• Primary Outcomes
  - PTSD Checklist
  - PHQ-9
  - AUDIT
  - SF-12/36 Physical Function
• Follow-up
  - 80% 3 month
  - 77% 6 month
  - 75% 12 month
TSOS Progress Implementation Aims
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?

**Follow-up**
How closely are participants followed-up?

**Primary outcome**
How relevant is it to participants?

**Primary analysis**
To what extent are all data included?

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

**Flexibility: delivery**
How should the intervention be delivered?
Original TSOS PRECIS-2 Wheel

- Eligibility
- Recruitment
- Setting
- Organization
- Flexibility Adherence
- Flexibility Delivery
- Follow-Up
- Primary Outcome
- Primary Analysis
From NIH Collaboratory ePCT Training Choosing Endpoints in PCTS (Richesson & Curtis 2/18):

- More pragmatic endpoints...
  - Matter to providers and patients
  - Are captured reliably as part of routine clinical care
  - Do not require central adjudication
  - Are shorter-term in nature
From NIH Collaboratory ePCT Training Choosing Endpoints in PCTS (Richesson & Curtis 2/18):

• More pragmatic endpoints...
  • Matter to providers and patients
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  • Do not require central adjudication
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Choosing an endpoint that is not captured reliably as part of routine clinical care or impedes the clinical workflow is not pragmatic!
Washington State Population Level Emergency Department Administrative Data on the Intent-to-Treat Sample

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.

Zatzick, Russo, Thomas et al 2018
TSOS PRECIS-2 Wheel

- Primary Analysis
- Recruitment
- Primary Outcome
- Setting
- Follow-Up
- Organization
- Flexibility Adherence
- Eligibility
- Flexibility Delivery
TSOS PRECIS-2 Wheel
Pragmatic Implementation Process Assessment: Methods Development

- Process assessments common in implementation science informed studies
- Often involve in-depth mixed methods
  - Semi-structured interviews
  - In-depth qualitative coding/analyses
- Not workflow integrated
TSOS PRECIS-2 Wheel
What Constitutes a Pragmatic Mixed Method for Implementation Process Assessments?

- Minimize cost per subject randomized
- Captured reliably as part of routine pragmatic trial roll-out
- Do not require central adjudication
Methods Development: Rapid Assessment Procedure Informed Clinical Ethnography (RAPICE*)

• TSOS research team spends hundreds of hours immersed in trauma care system clinical context
• Front line clinician-researcher conducts participant observation
• Field notes & jottings taken, logs recorded
• Field data regularly reviewed (e.g., monthly) with mixed-method expert consultant
• Themes related to trial roll-out and sustainable implementation iteratively discussed & documented
• RAPICE procedures do not drive up costs of trial

*Palinkas & Zatzick ADPM, 2018
TSOS PRECIS-2 Wheel

Primary Analysis
Primary Outcome
Follow-Up
Flexibility Adherence
Flexibility Delivery
Setting
Organization
Recruitment
Eligibility
TSOS RAPICE Implementation Process Assessment: Preliminary Findings

- Recurrent intervention and research staff turnover across sites
- Consistent observation that some patients do not engage in the intervention
- Implementation process assessment informs a priori secondary hypotheses that suggest per protocol modifications to the original ITT analyses
Trauma Survivors Outcomes & Support (TSOS) PRECIS-2 Wheel
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Trauma Survivors Outcomes & Support (TSOS) PRECIS-2 Wheel
Summary: TSOS Progress on Effectiveness & Implementation Aims

- Effectiveness
  - Baseline data cleaned and analyses have begun
  - Follow-up interviews ongoing with 75-80% completion
- Implementation
  - Pragmatic implementation process methods developed
  - TSOS implementation process assessment ongoing
  - Key implications for multiple TSOS PRECIS-2 domains