Civilian Trauma Centers are a Cost-Effective, Military-Relevant, and Feasible Platform for Acute Stress Reaction Interventions

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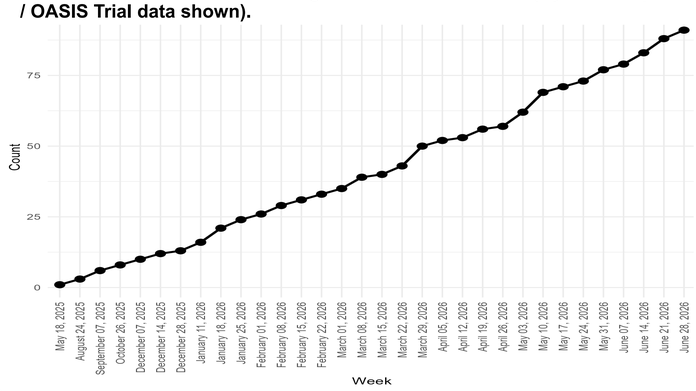
Introduction

- Stress reactions degrade decision-making, cognitive function, and mission performance. Advances in neuroscience are yielding many new promising interventions to reduce/extinguish stress reaction symptoms and restore neurocognitive performance.
- **Identifying effective interventions, and successfully integrating them into warfighting, is critical to maintaining performance overmatch against near-peer military rivals.**
- Identifying such interventions requires the development of cost-effective, high-throughput, high-fidelity intervention proving/testing grounds.
- We demonstrate the feasibility of the AURORA research network, a civilian emergency department-based intervention testing network, to assess candidate interventions to extinguish stress reaction symptoms and restore neurocognitive function.

Examples

- Examples of different types of interventions tested in motor vehicle collision survivors experiencing stress reaction symptoms using the network
  1. Behavioral (**iCOVER**)
     - *Adults with stress reactions randomized in the ED to iCOVER, usual care, or physical presence with reassurance. Ongoing,~400 enrolled*
  2. Pharmacological (**Cyclobenzaprine, OASIS**)
     - *Adults presenting within 72 hours of a motor vehicle collision are randomized to nightly sublingual cyclobenzaprine or placebo for two weeks* (**Figure 1**) *Ongoing, > 105 enrolled*
  3. Psychological (**Written Exposure Therapy, WISE**)
     - *Adults with stress reaction after motor vehicle collision randomized to 5 weekly sessions of written exposure therapy vs. control (pilot)*

Figure 2. Trials achieve steady recruitment of at least 15-20 trauma survivors per month experiencing acute stress reactions. (Cyclobenzaprine / OASIS Trial data shown).



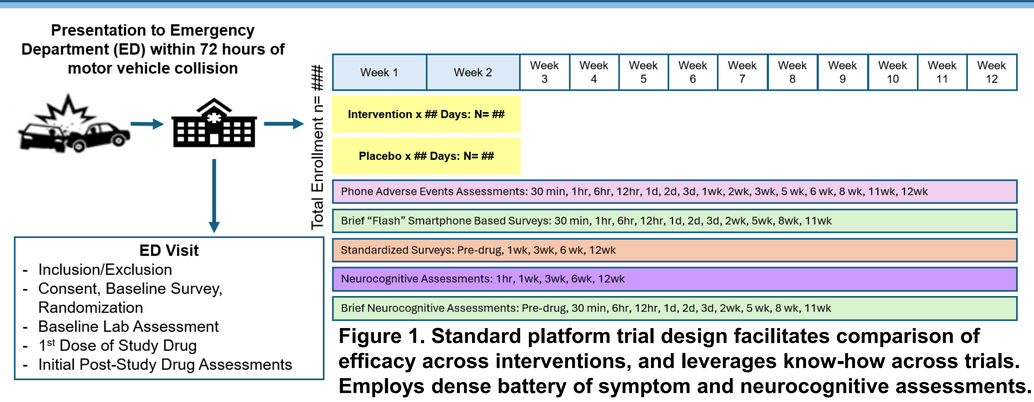


Figure 1. Standard platform trial design facilitates comparison of efficacy across interventions, and leverages know-how across trials. Employs dense battery of symptom and neurocognitive assessments.

Figure 3. Patient flow shows feasibility across AURORA Research Network intervention trials

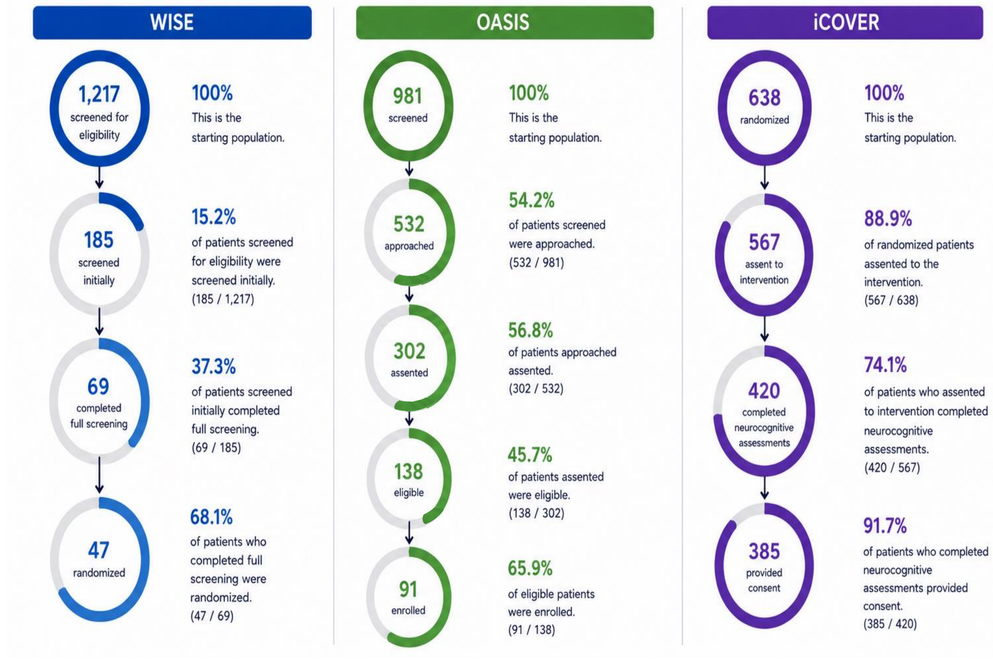


Table 1. Trials successful in recruiting trauma survivors who are experiencing substantial stress reaction symptoms in the hours after trauma (i.e., 12 or more stress reaction symptoms).

Cyclobenzaprine/OASIS (data from when n=91)	
Mean number of ASR symptoms (0-23) reported immediately after trauma	12.55 (7.08)
Mean number of moderate-severe ASR symptoms (0-23) reported immediately after trauma	8.86 (7.04)
Written exposure therapy trial (n = 41)	
Peritraumatic distress inventory raw score immediately after trauma	15.56 (7.11)
Percent of recruited trauma survivors with substantial peritraumatic distress (>9) immediately after trauma	83%

Results

- All three intervention trials demonstrate strong feasibility, including high participant approach and enrollment (**Figures 2 & 3**), adherence, and follow-up rates
- Adverse events have been limited and predominantly mild across all trials
- Enrolled patients resemble military populations sociodemographically and exhibit high levels of ASR symptoms (**Table 2**), ***supporting the military relevance of these civilian trauma cohorts***
- Per participant costs at civilian ED sites > 3 times less than recruitment from military sites, and lower concern for symptom underreporting. (Military sites optimal to include as subset of enrollees.)

Conclusions

- The AURORA network provides a high-throughput, high-fidelity, relatively low-cost intervention testing grounds for stress reaction interventions. The network provides a critical pathway to accelerate identification of effective interventions that preserve and optimize warfighter performance

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