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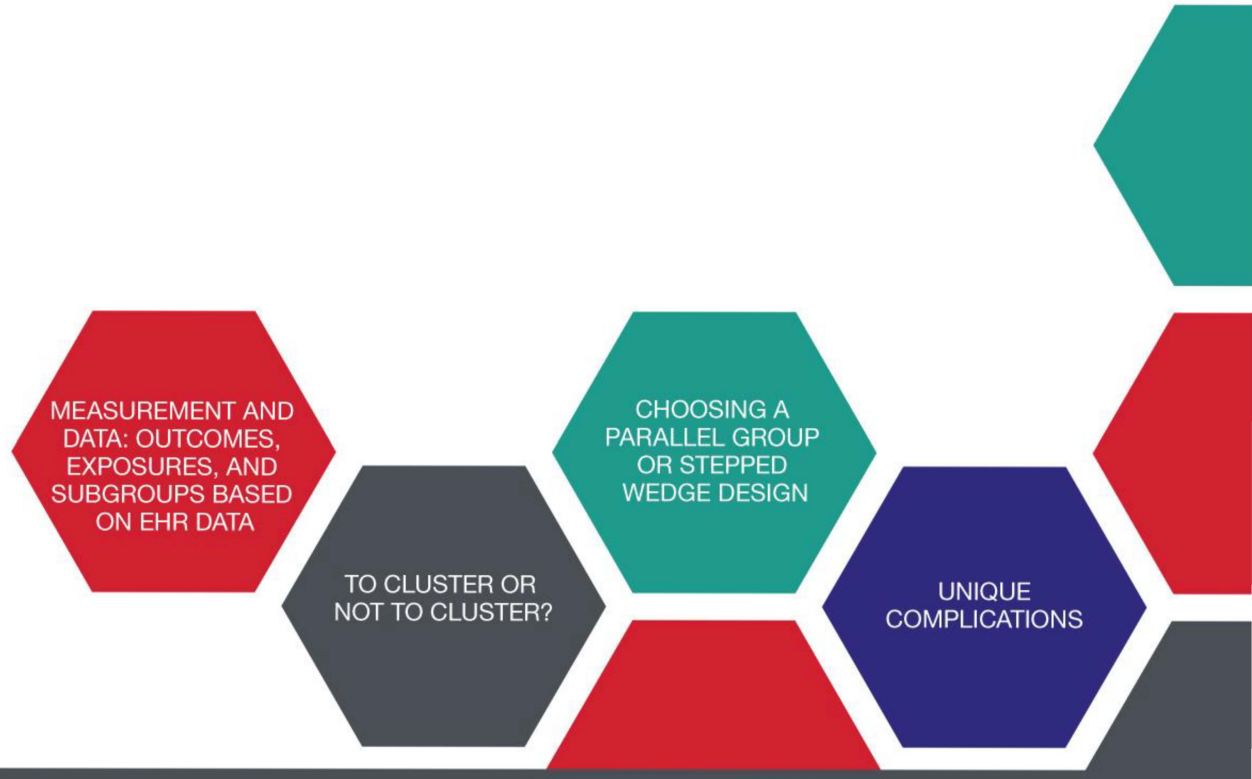
Design & Analysis of Embedded

Pragmatic Clinical Trials



Panel 3:
Choosing a Parallel Group or Step Wedge Design

Lumbar Imaging with Reporting of Epidemiology (LIRE)

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UH2 AT007766-01; UH3 AT007766

Intervention

- Insertion into L-spine imaging reports prevalence data for common findings in pts without back pain

EXAMPLE: The following findings are so common in normal, pain-free volunteers, that while we report their presence, they must be interpreted with caution and in the context of the clinical situation. Among people between the age of 40 and 60 years, who do not have back pain, a plain film x-ray will find that about:

8 in 10 have disk degeneration

6 in 10 have disk height loss

Note that even 3 in 10 means that the finding is quite common in people without back pain.

Primary Outcome

- Overall spine-related healthcare as measured by spine-related relative value units (RVUs) ascertained from EMR

Trial Specific Problem Related to Stepped Wedge

- Non-implementation of intervention due to
  - Technical delay
  - Refusal of clinic to participate after randomization

Addressing the Problem

- Technical delay
  - Work with site PI to troubleshoot the technical problem
  - Required active engagement of programmers
- Refusal of clinic to participate after randomization
  - Work with site PI to troubleshoot the social/political problem
  - Compromise → minor change to intervention text

Problem Resolution

- Technical delay
  - Resolved problem within 1 month delaying initial implementation (lucky- no x-over)
- Refusal of clinic to participate after randomization
  - Site agreed to revised text and participated after 6 week delay
  - This did result in x-over

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EMBED:
PRAGMATIC TRIAL OF USER-CENTERED CLINICAL DECISION SUPPORT TO IMPLEMENT EMERGENCY DEPARTMENT-INITIATED BUPRENORPHINE FOR OPIOID USE DISORDER

Design change from Stepped Wedge to Group Randomized

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Yale SCHOOL OF MEDICINE

Intervention and Primary Outcome

- **Setting**: 20 Emergency Departments (EDs) across five healthcare systems over 18 months
- **Population**: Adult ED patients (age 18 years or older) discharged from the ED with OUD. Patients currently pregnant or taking a medication for OUD will be excluded.
- **Intervention**: The intervention consists of a user-centered CDS integrated into ED clinician electronic workflow and available for guidance to: 1) determine whether patients presenting to the ED meet criteria for OUD, 2) assess withdrawal symptoms, and 3) ascertain and motivate patient willingness to initiate treatment. The CDS guides the ED clinician to initiate buprenorphine and facilitate follow up.
- **Primary Outcome**: Initiation of BUP in the ED (Y/N) defined as whether or not an eligible patient is administered BUP in the ED and/or prescribed BUP upon discharge from the ED. Ascertained via EHR.

Problem: Stepped Wedge vs Parallel Group CRT

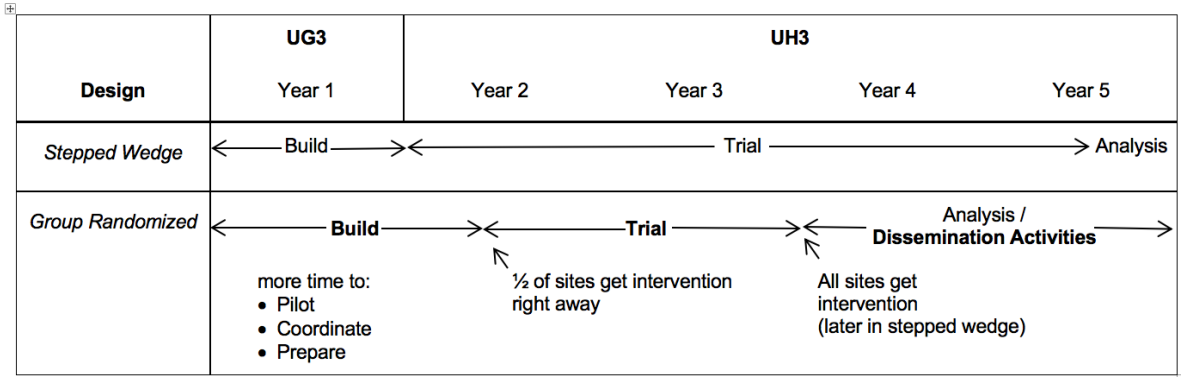
- **Integration/implementation of CDS was site specific and required substantial resources.**
- **Sample size issues: small number of clusters to enroll, poor identification of patients that may benefit from intervention, variable volume of eligible patients.**
- **Control of heterogeneity.**
- **Concern for temporal trends as care for OUD is changing.**
- **Study timeline.**

Comparing Features of the 2 Designs

Feature	Stepped Wedge	Group Randomized
Length of trial	Longer trial period due to baseline and post-implementation phases	Shorter trial period
Control for temporal trends	Weaker, more vulnerable due to longer trial period	Stronger, due to shorter trial period
Control of heterogeneity by site	Yes, sites serve as their own control	Not as good, compensate for this weakness by employing constrained randomization
All sites get intervention	Yes	No, but can offer at end of shorter trial
Number of clusters (ED sites)	Fewer	More (necessitating this supplement request)
Go-live of IT intervention	Staggered, later implementations can learn for issues in earlier ones	Synchronized, requires more lead time and coordination
Additional time for IT build, pilot testing, and dissemination	No, due to longer trial period	Yes, shorter trial period permits additional time for IT build and dissemination in later UH3 years

Resolution

- Increasing the CDS build and integration period allowed for the switch to a group randomized CRT.
- Provided better control of temporal trends.
- Resulted in shorter overall trial period.
- A larger number of EDs were required to maintain power.
- Covariate constrained randomization used for balance across interventions.
- Offer all EDs intervention at end of trial.



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Parallel Group or Stepped Wedge Design? Lessons Learned from the Trauma Survivors Outcomes & Support (TSOS) Pragmatic Trial

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Funded by Grant UH3 MH106338

TSOS Intervention & Primary Outcomes

- Intervention: Multifaceted collaborative care intervention that includes care management, behavioral interventions, and pharmacotherapy targeting posttraumatic stress disorder (PTSD) and related comorbidity.
- Primary Outcomes:
  - PTSD symptoms (PTSD Checklist)
  - Depressive symptoms (PHQ-9)
  - Alcohol use (AUDIT)
  - Physical function (MOS SF-36)

Key TSOS Questions

- Were there dissemination and implementation considerations/associated ethical issues related to adopting a particular design?
- How was potential intervention effect/site heterogeneity considered in the design and analysis of the study?

Key TSOS Considerations

- Prior parallel group 20 trauma center pragmatic trial (DO-SBIS)
- All sites want/request training
- Marked 25 site heterogeneity across multiple domains
  - Geography: Urban/inner city sites associated with violent injury
  - Center admission volume: Impacts recruitment rates
  - EHR: Information exchanges/ associated with better linkages

Lessons Learned: TSOS Shift to Stepped Wedge Design

- Addresses issues related to training and site contribution to intervention and control conditions
- Stepped wedge more vulnerable to site variability in recruitment rates and other pragmatic trial issues (regulatory delays)

Questions and Answers

Please submit questions for the panelists to:

PragClinTrialsWkshp@mail.nih.gov