
Welcome
47TH
Annual Meeting
PHOENIX
May 17-20, 2026
SCT
SOCIETY FOR CLINICAL TRIALS

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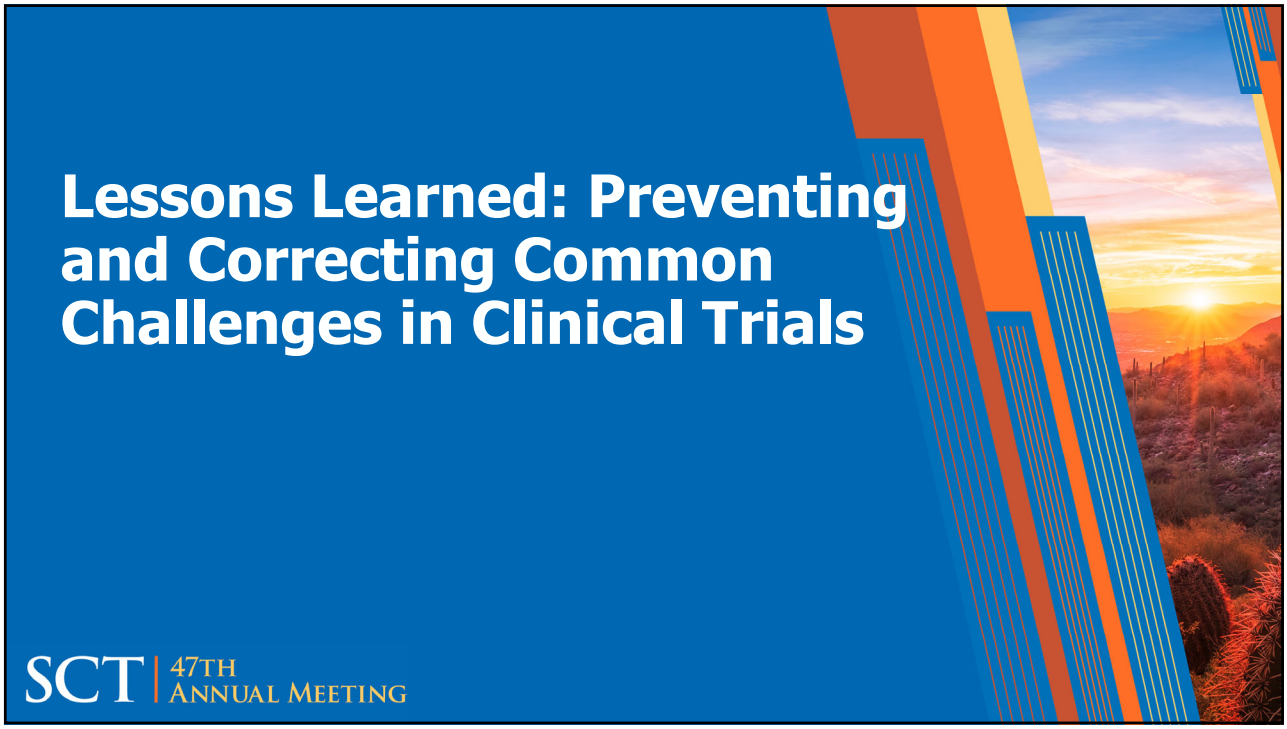
Lessons Learned: Preventing and Correcting Common Challenges in Clinical Trials
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Presenters

- **Sally Jo Zuspan,** RN MSN, Utah Data Coordinating Center, University of Utah
- **Michelle Lancet**, BS, Center for Biostatistics & Qualitative Methodology, University of Pittsburgh
- **Bryan Blette**, PhD, Department of Biostatistics, Vanderbilt University Medical Center
- **Brian Mittman**, PhD, Department of Research and Evaluation, Kaiser Permanente Southern California
- **Dixie Ecklund**, RN, MSN MBA, Clinical Trials Statistical and Data Management Center, University of Iowa

Moderator: **Barbara H. Braffett**, PhD, The Biostatistics Center, The George Washington University

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UNICORN Network

- Academic Data Coordinating Centers (DCCs) provide collaborative leadership in multi-site clinical research studies.
- The **UNI**versity data **CO**o**R**dinating ce**N**ters (UNICORN) Network convenes members of academic institutions leading DCC activities to advance the discipline of data coordination.

DCC's are excellent resources on how to improve the rigor and impact of clinical research.
We are advocates for best practices of study design, DCC activities, and statistical analysis.
This presentation highlights how DCC's think and solve common problems.

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UNICORN
UNIversity data COoRdinating ceNters

https://unicorn-dcc.org/

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Disclosures

- No relevant disclosures

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Where do Things go Wrong in Clinical Trials?

Our Focus:

- "Standard of care" & variability at clinical sites
- Regulatory adherence
- Randomization & enrollment
- Complex health interventions
- Investigational product tracking

Chat GPT Says:

1. Protocol conduct / protocol adherence failures
2. Data integrity, source documentation, and endpoint verifiability failures
3. Eligibility and enrollment integrity failures
4. Safety reporting and human-subject protection failures
5. Treatment adherence, retention, and missing-outcome-data failures

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Variation in Clinical Care….
How will it impact your Trial?

Sally Jo Zuspan RN, MSN
University of Utah Data Coordinating Center
Salt Lake City, Utah

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When Standard of Care is not…Standard

- In multicenter trials, sites ~~may~~ will implement same protocol differently
- This ~~can~~ will affect enrollment, procedures, adherence, endpoints, safety, and data comparability.
- **Today we will talk about:**
  - How variability in 'usual care' creates *predictable and unpredictable* implementation problems.

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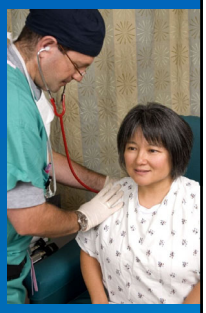
Background and Why This Matters

- Even well-trained, committed sites drift because sites differ in:
  - clinical workflow, staffing
  - timing of standard procedures
  - documentation habits
  - local standards of care
- **Site variability is not "noncompliance".** It is a mismatch between protocol assumptions and real-world site practice.
- Your mission: to find these early and define, standardize, and measure them.



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The Problem: Assumptions made about 'usual care'

Case 1: No standardization for BP (eligibility, secondary aim)

Trial requires "routine BP monitoring per SOC" before each dose.

- Site A-measures BP after 5 minutes seated, using automated cuff.
- Site B-takes BP immediately after rooming patient using manual cuff.
- Site C-BP not standard; uses inpatient vitals from EHR if within the same day.
- **Impact:** Eligibility, outcomes, safety.

15–30% difference

Case 2: Interpretation of Eligibility

Excludes patients with "clinically significant cognitive impairment."

- Site A-formal MoCA score cutoff.
- Site B-physician judgment.
- Site C-excludes documented dementia diagnosis but includes patients with mild impairment.
- **Impact:** Population differs across sites. Affects safety, adherence, endpoint, missing data, and generalizability.

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What Does the Literature Say?

- Turner et.al.-'usual care' in pragmatic trials *should not be treated as uniform*; can vary by patient clinician, site, health system and time.
- Ayling et.al. SOC conditions were often 'poorly described', making it difficult to know what participants actually received or how the control group different from the intervention group.

"Per SOC" should trigger a design question:
What exactly is allowed to vary and what must be standardized or described or monitored?

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Turner et.al. Defining usual care comparators when designing pragmatic trials of complex health interventions: a methodology review. Trials. 2024 Feb 12;25(1):117.

Ayling, et.al. How Standard is Standard of Care?. Psychol Health. 2015 Jan;30(1):85-103

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Variation is expected; *unmanaged* variation is the problem

undetected

- Screening & Eligibility-Inconsistent application of inc/exc criteria
- SOC Pathways- local order sets, clinic flow, referral timing
- Procedures-labs, imaging, specimen handling, visit windows
- Safety-thresholds for escalation, varying dx tests will affect detection of S/AEs

Site workarounds don't get communicated to the coordinating center

If variability exists, it impacts every aspect of the trial

Key for outcome variables, but also others!

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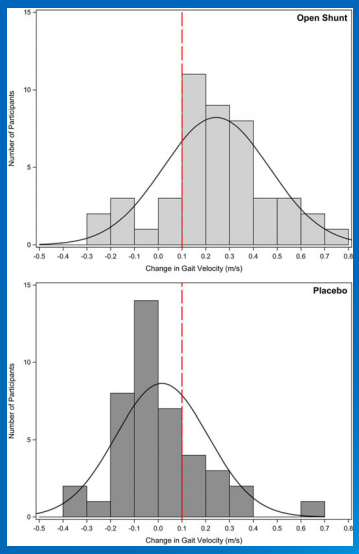
A Randomized Trial of Shunting for Idiopathic Normal-Pressure Hydrocephalus

- Double-blind, randomized, placebo-controlled trial; participants selected for shunt surgery. Primary outcome-change in gait velocity at 3 months.
- 99 patients, 20 sites US & Canada and 1 European site
- DCC-University of Utah; CCC-Johns Hopkins University
- *Shunting resulted in significant improvements at 3 months in gait velocity.*
- When the outcome is "usual care".



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Funded by the National Institute of Neurological Disorders and Stroke and the Trial Innovation Network; ClinicalTrials.gov number, NCT05081128.
Luciano et. Al. A Randomized Trial of Shunting for Idiopathic Normal-Pressure Hydrocephalus. 2025. N Engl J Med

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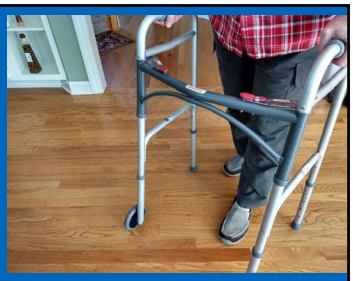
Practical Application-Gait Analysis



- Primary outcome is change in gait velocity using 10M walk test.
- 10 walk test is simple & widely used across US and Canada.
- Strong validity* across neurologic patients; Excellent reliability
- ICC ranging from .87 to .99 across studies ** (scores consistent across testers)
- Safe, easy, and inexpensive to administer

What could go wrong? Do you see any risks?

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*Cheng DK, et al. Top Stroke Rehabil. 2020. **Green et al., Clinical Rehab 2002. Cleland et al., Physiotherapy Theory and practice 2020.

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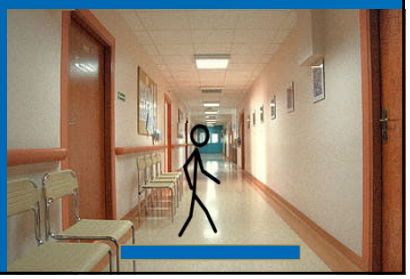
What is standard about your outcome?

- What is *standard* about 10M walk test?
  - Distance (10M)* (*mostly!)
  - Measurement (m/sec)
  - Average of 3 trials is often used
  - Equipment-stopwatch, marked walkway (tape on floor)
  - Standard phrasing "walk at your normal pace".
  - Assistive devices allowed but kept consistent



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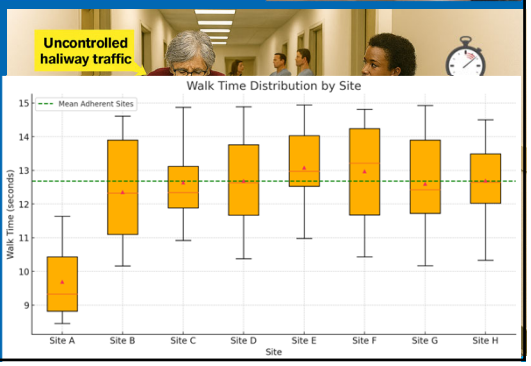
The Pilot & "Usual Care": What we knew

- Registry data*→Pilot data from small trial
  - Static vs dynamic start
  - Number of trials per gait exam
  - Busy clinic and staffing leads to variation:
    - Instructions, footwear, environment
  - Assistive devices (cane, walker, orthotics)
  - Patient fatigue (walking to appointment, meds, testing)
  - Verify walkway length*



*Adult Hydrocephalus Clinical Research Network

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But What about Randomization?

- Randomization balances patients but does not make care uniform.
- Even with randomization, a trial can be comparing the intervention to different versions of "usual care", shrinking the treatment effect. If other sites provide minimal usual care, the effect may look larger.

Post Stroke Cognitive Recovery Trial

PI says "Cognitive screening and rehab referral are SOC"

Site	Actual Usual care
Sites A–C	Formal cognitive screening, occupational therapy evaluation, and automatic referral to cognitive rehab if impaired.
Sites D–G	Cognitive concerns are addressed only if the treating clinician notices a problem.
Sites H–J	Screening is inconsistent and rehab referral depends on staffing, insurance, and discharge destination.

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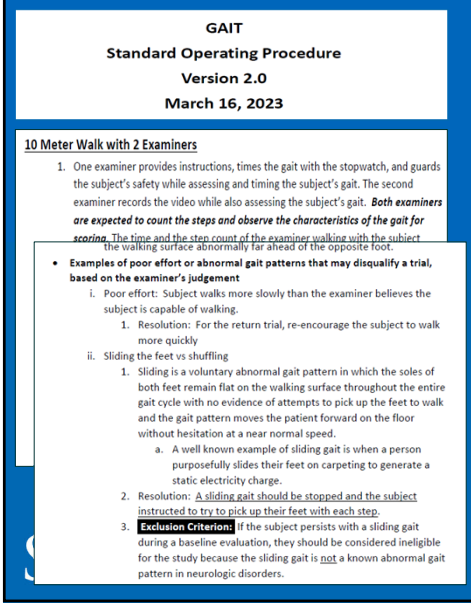
Define, Standardize, and Measure



GAIT
Standard Operating Procedure
Version 2.0
March 16, 2023

10 Meter Walk with 2 Examiners

1. One examiner provides instructions, times the gait with the stopwatch, and guards the subject's safety while assessing and timing the subject's gait. The second examiner records the video while also assessing the subject's gait. ***Both examiners are expected to count the steps and observe the characteristics of the gait for scoring.*** The time and the step count of the examiner walking with the subject the walking surface abnormally far ahead of the opposite foot.

- **Examples of poor effort or abnormal gait patterns that may disqualify a trial, based on the examiner's judgement**
  - i. Poor effort: Subject walks more slowly than the examiner believes the subject is capable of walking.
    1. Resolution: For the return trial, re-encourage the subject to walk more quickly
  - ii. Sliding the feet vs shuffling
    1. Sliding is a voluntary abnormal gait pattern in which the soles of both feet remain flat on the walking surface throughout the entire gait cycle with no evidence of attempts to pick up the feet to walk and the gait pattern moves the patient forward on the floor without hesitation at a near normal speed.
       a. A well known example of sliding gait is when a person purposefully slides their feet on carpeting to generate a static electricity charge.
    2. Resolution: A sliding gait should be stopped and the subject instructed to try to pick up their feet with each step.
    3. **Exclusion Criterion:** If the subject persists with a sliding gait during a baseline evaluation, they should be considered ineligible for the study because the sliding gait is not a known abnormal gait pattern in neurologic disorders.

- Define & standardize gait testing workflow
  - Gait SOP (CCC)
  - Mandatory video-taping of gait testing for qualification, certification, and ongoing monitoring
  - Standardized gait scoring tool (CCC & DCC)
- Measure the data (compliance, outcome)
  - Data collection form evaluating each gait trial (DCC)
  - Central Gait Core (CCC)
  - Regular reporting on gait compliance (DCC)
- Continue to monitor
  - DCC-Remote and onsite monitoring-(DCC)
  - Feedback to site (CCC)

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Key Takeaway

- Standard/usual care is not automatically uniform in trials.
- You must **define, standardize, and measure it.**
- Differences in what participants receive can affect interpretation, reproducibility, and treatment effect.

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Lessons Learned: Preventing and Correcting Common Challenges in Clinical Trials

The Challenges of Regulatory Compliance

Michelle Lancet
University of Pittsburgh
Center for Biostatistics and Qualitative Methodology (CBQM)

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Regulatory Compliance: Your Trial's Guardrail

"Is this really a big deal?"

-research coordinator who shall not be named

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Regulatory Challenges: Clear and Present Danger (to our blood pressure)

Collection and Storage Methods of Site-Level Records

-Lack of regulatory coordinators

-Delay in collection causes more delays in site or personnel activation

-Sites were not using regulatory software

Complexity of Document Management

-Training requirements for role specific tasks and protocol

Site activation: initial activation and ongoing maintenance

-Team size and personnel turnover

Coordinating Center and Site Level Pain Points

-Tracking burden of expired documents

-Multi-Center strain

-Resource constraints

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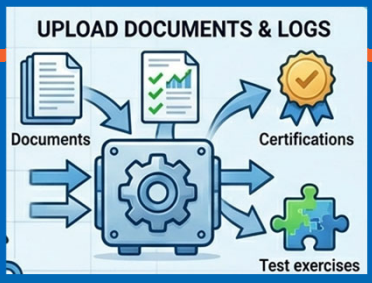
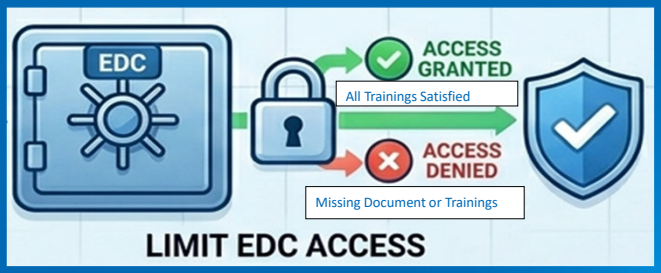
Designing an Electronic Master Regulatory File





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Role Requirements and Document Upload

Access to EDC and Authorities Identified

Will this individual require access to the STUDY web-based electronic data capture system (eSYSDM)?
(•) Yes ( ) No

Investigator Participation

Is this Investigator to be listed on the Delegation of Authority?
(•) Yes ( ) No

Delegation of Authority

☑ The Principal Investigator is responsible for all research procedures outlined below

Select the responsibilities delegated by the PI to this Investigator from the list of study activities below.

- ☐ 1. Subject selection, recruitment, scheduling appointments and follow up contact
- ☐ 2. Obtain informed consent
- ☐ 3. Confirm eligibility (inclusion/exclusion criteria)
- ☐ 4. Obtain medical history
- ☐ 5. Perform physical exam/Clinical Evaluations
- ☐ 6. Review of Vitals/labs for clinical significance
- ☐ 7. Determine study related medical decisions
- ☐ 8. Assess Adverse Events/SAEs
- ☐ 9. Prescribe study drug
- ☐ 10. Administer/dispense study drug
- ☐ 11. Investigational product accountability/storage
- ☐ 12. Sample collection/processing
- ☐ 13. Sign-off on (e)CRFs
- ☐ 14. Maintain essential documents/ data entry/queries/corrections
- ☐ 15. Regulatory Management/IRB submissions
- ☐ 16. Project Management

Document Upload Function

Curriculum Vitae (CV)

Upload a current CV for the investigator. The document must be signed and dated in the top right hand corner of page 1. The CV is considered current within **2 years** of signed date.

Provide a current copy of the Investigator's CV with signature and date in top right hand corner of document.
Choose File No file chosen

Date Signed: (MM/DD/YYYY)

Date Uploaded	Uploaded By	Date Signed:	Expiration Date		Status
4/24/2025	[redacted]	4/24/2025	4/24/2027	Review Document	Accepted
1/31/2023		1/23/2023	1/22/2025	Review Document	

Medical License

Provide a copy of the Investigator's State (CT) Medical License.
Choose File No file chosen

Expiration Date: (MM/DD/YYYY)

Date Uploaded	Uploaded By	Expiration Date		Status
1/14/2026	[redacted]	12/31/2026	Review Document	Accepted
3/16/2025		12/31/2025	Review Document	Accepted

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Site Summary Report

Active Personnel

Expired Documents

Name	CV (Expiration Date)	Medical License (Expiration Date)	Financial Disclosure (Expiration Date)	1572	Delegation of Authority	GCP (Expiration Date)	Human Subject Research (Expiration Date)	SIV/Alternative Training	Cultural Competency Training	Nurse Navigator Training	Pharmacist Training	Telemedicine Training
[redacted] MD MS Principal Investigator	4/24/2027	12/31/2026	N/A		✓	4/28/2026	4/28/2028	8/30/2023	N/A	N/A	N/A	4/14/2023
[redacted] MD PhD MBBS/FASN Co-Investigator	4/24/2027	11/30/2025	N/A		✓	3/10/2027	3/10/2027	8/30/2023	N/A	N/A	N/A	N/A
[redacted] Lead Coordinator;Site Registrar	N/A	N/A	N/A		✓	4/24/2028	1					
[redacted] Research Coordinator	N/A	N/A	N/A		✓	5/15/2026	1					
[redacted] Regulatory Manager	N/A	N/A	N/A		✓	6/6/2026	9					

Example Email Alert for Expired Documents

Hi,

This notice is to alert you to study team member(s) or departmental credentialing or certifications that are either expired or are pending expiration. Please obtain updated versions from the study team members listed below and upload the new versions into the KPoP eMRF system as soon as current documentation becomes available.

Site: VCU - Virginia Commonwealth University

STUDY TEAM MEMBER NAME	STUDY TEAM ROLE	Expiring/Expired Document	Date of Expiration
[redacted]	Principal Investigator	COI	5/30/2026
[redacted]	Principal Investigator	COI	5/30/2026
[redacted]	Lead Coordinator	GCP	5/26/2026

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Key Takeaways

- We cannot underestimate the impact that regulatory compliance has on the safety of our participants and the consistency and quality of your trial data.
- Training requirements, certifications, recertifications, and verification of staff qualifications yields higher fidelity to protocol.
- Use of an eMRF reduces burden on both DCC and CCC to keep regulatory compliance current.

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Acknowledgments

CBQM eMRF and EDC Programmers

Joseph Weiss
Kyle Holleran
Yanxue Tong
Jason Kojtek
Dave Yankovich

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Lessons Learned: Unexpected Issues in Surgery Trials

BRYAN BLETTE
VANDERBILT UNIVERSITY MEDICAL CENTER

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Overview

- Surgical interventions and innovations can greatly improve outcomes, and randomized clinical trials are feasible as a gold-standard study design for their evaluation
- However, surgery is very different from drugs, educational programs, or other common trial interventions

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Case Study

- Population: Patients receiving surgery who will have long-term healing of skin or other tissue post-procedure
- Intervention: Novel version of temporary device to improve and hasten healing of tissue
- Outcome: Time until tissue is fully healed

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Surgical Trials Can Have Unexpected Issues

- Some common issues include:
  - Inability to blind the surgeon (e.g., new surgical technique)
  - Inability to blind patients (e.g., visible implanted device)
  - Issues in standardization across participating surgeons
  - Issues during procedure unrelated to the intervention

While we anticipated the above issues, there were several challenges we did not anticipate

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Challenge #1: Eligibility

Patients need to be randomized prior to surgery to ensure device is properly prepared for the procedure

However, inclusion criteria include knowledge of the surgical area anatomy that is unknown until surgery

Therefore, in these trials, it may be necessary for randomization to occur before inclusion criteria are full assessed

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Challenge #1: Eligibility

Problem: If we include the patients in analyses, it feels non-sensical. If we exclude them, then we fail to adhere to the specified ITT framework (treatment policy strategy)

Solution: Protocol amendment to change to a modified ITT strategy – exclude patients who are randomized but fail to meet the final inclusion criterion

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Challenge #2: Patient Interest

As in many trials, we have experienced a lower rate of enrollment than expected

We also had higher drop-out than expected – surgical patients with better recovery have less incentive to follow-up

Discussion with coordinators indicated that the follow-up schedule was too burdensome for patients

Unified solution: Protocol amendment to streamline (reduce) follow-up visits

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Challenge #3: Validity of Primary Endpoint

- "Healing of tissue" can be defined in many different ways
- In one of our trials, we defined it as time until readiness for a skin graft
- However, due to other changes in standard clinical care in the population, skin graft was not recommended for patients who experienced substantial healing

This created a paradoxical issue – patients with the best healing post-surgery were not eligible to achieve the pre-specified primary outcome

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Challenge #3: Validity of Primary Endpoint

- **Solution:** We had a pre-specified secondary outcome that used imaging technology to measure tissue healing directly. We proposed to switch the primary and secondary outcome since the secondary outcome became more relevant with these changes

- **Nuances:** Need to make a rigorous justification for IRB/FDA, trying to show that we did not change the primary endpoint to save a failing trial

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Lessons Learned

- Amendments exist for a reason – it's hard to anticipate all potential challenges that will occur in a trial
- PIs can be overly optimistic about patient enthusiasm – it can be better to anticipate lower interest and use a leaner design and remote data collection as long as it doesn't impair the study
- Traditional primary endpoints are not always valid if a novel intervention changes the body's response to surgery

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Stats Problems vs. DCC Problems

- The 3 challenges discussed are relevant to both trial statisticians and data coordinating centers
- Integration of statisticians within DCCs is key to fast resolution of unexpected issues in trials

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Challenges in Clinical Trials of Complex Health Interventions:

Strengthening Study Coordination and Follow-up

May 19, 2026

Brian S. Mittman, PhD

Department of Research and Evaluation
Kaiser Permanente Southern California

Clinical and Translational Science Institute
University of California at Los Angeles

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Overview

1. Case study: challenges in coordinating a portfolio of HPV vaccination improvement studies to maximize *value*
2. Complex health interventions: definition, features, evaluation challenges
3. Complex health interventions: coordination challenges
4. Summary: recommendations to enhance evaluation, coordination and follow-up (*value*)

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Key messages

1. Complex health interventions are different from simple interventions: their unique features pose challenges and unique requirements for evaluation and for harmonization, synthesis and coordination
2. Harmonizing and coordinating complex health interventions requires additional coordination services (coordinating center roles and responsibilities) relative to simple interventions

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Challenges in evaluating and coordinating studies to improve HPV vaccination rates: *The scourge of extreme heterogeneity*

Intervention, evaluation

- Heterogeneous intervention elements *(comparison, synthesis)*
- Varying availability of intermediate outcomes, mediators, moderators, process data *(explanation, comparison, synthesis)*

External context

- Varying scope-of-practice, registry policies
- Varying interest group engagement
- Staggered discovery of (response to) new social media messaging, regulations, pharma company donations

Findings, follow up

- Extreme heterogeneity in results
- Variable documentation, reporting (replication, adoption)
- Diverse patterns of follow up (unrelated to findings)

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HPV vaccination improvement programs are complex health interventions

- Multiple, interacting components
- Intervention targets multiple levels, entities
- Intervention is adaptable (tailorable)
- Intervention effects occur through multiple mediated, moderated causal pathways
- Examples: health promotion programs, healthcare delivery innovations, implementation/improvement bundles

Craig et al, BMJ 2008;337:a1655.
Guise et al, JClinEpi 2017;97:6

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Simple vs. complex health interventions

Simple interventions

Single fixed (stable, homogeneous) targeting
A single (relatively) stable process to achieve
A distinct goal within
Stable, (relatively) homogeneous settings
Relative simplicity, stability, homogeneity, consistent (often strong) main effects

Complex health interventions

Multiple varying activities deployed at
Multiple levels targeting
Multiple structures and processes to achieve
Multiple (conflicting) goals within
Dynamic, heterogeneous settings
Extreme complexity, instability, heterogeneity, variable (often weak) main effects

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Challenges in evaluating and coordinating studies to improve HPV vaccination rates: *The scourge of extreme heterogeneity*

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Solutions to challenges in coordinating CHI studies

Comparison, synthesis

- Harmonize interventions (via core function/form framework)
- Develop, harmonize theory-based causal models (to guide harmonized evaluation)
- Harmonize data collection and analysis plans (including intermediate outcomes, mediators, moderators)

Reporting, dissemination, follow up

- Coordinate (and enhance) stakeholder engagement
- Harmonize (and enhance) reporting, dissemination (content, format, channels)

Additional coordination services

- Shared learning

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Core functions and forms

- **Core Function**: purpose, intended effect(s); linked to needs
- **Form**: activity, format, operationalization

Hawe P, Shiell A, Riley T. Complex interventions: how "out of control" can a randomised controlled trial be? *BMJ*. 2004 Jun 26;328(7455):1561-3.

Hawe P. Lessons from complex interventions to improve health. *Ann Rev Public Health*. 2015 Mar 18;36:307-23.

Perez Jolles M, Lengnick-Hall R, Mittman BS. Core functions and forms of complex health interventions. *J Gen Intern Med*. 2019 Jun; 34(6):1032-1038.

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Core functions vs. forms

- Physical activity forms: walking, running, swimming
- Patient education forms: printed materials, videos, nurse education, MD education, peer education
- Inpatient stay information transfer (care transitions interventions) forms: shared EHR, discharge summary, faxed/mailed/emailed/hand-carried letter
- Smoking cessation core functions: nicotine replacement, motivation, support

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Ongoing work to strengthen CHI research and evaluation, coordination and harmonization, and follow-up

1. Develop and refine a CHI RCC framework (CF/F matrix) and guidance
2. Test the *coordination hypothesis*
3. Develop guidance for enhanced and coordinated engagement, dissemination and follow up
4. Accelerate and guide pharma/life science industry entry into healthcare delivery science
5. Accelerate and guide patient advocacy organization, philanthropic foundation and specialty society entry into healthcare delivery, health promotion science

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Thank you

Brian.S.Mittman@kp.org

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Investigational Product Management in Clinical Trials

Dixie J. Ecklund, RN, MSN, MBA
Clinical Trials Statistical & Data Management Center
University of Iowa
dixie-ecklund@uiowa.edu

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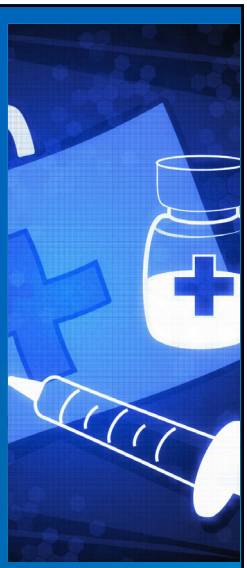
Why is IP Management Important?



Drug Supply Monitoring

Close monitoring of drug supply ensures treatment continuity and supports recruitment and retention in trials.

Inventory Control and Safety

Accurate inventory control prevents expired product use, ensuring patient safety and regulatory compliance.

Randomization and Bias Minimization

Proper randomization protects trial validity by minimizing bias in drug assignment.

Drug Accountability and Compliance

Monitoring drug accountability confirms dosing accuracy/participant adherence to regimens.

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What Is at Risk?

Data Integrity Risks
Incomplete or inaccurate dosing records threaten data integrity and undermine study efficacy and safety analyses.

Patient Safety Risks
Incorrect dosing and improper handling increase risks to patient safety, especially in complex treatment regimens.

Regulatory Compliance Risks
Mishandled accountability logs and broken blinding can lead to audit findings and delays in regulatory inspections.

Timelines and Financial Risks
Drug shortages and corrective actions delay study timelines and increase costs, risking sponsor trust and reputation.

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Why This Issue Is Especially Relevant Now

Rising Complexity of Investigational Products
Investigational products now include biologics, gene therapies, and require cold-chain logistics, increasing operational challenges.

Budget and Efficiency Pressures
Funders demand budget cuts and greater operational efficiency without sacrificing clinical trial quality and compliance.

Role of Academic DCCs
Academic DCCs offer centralized infrastructure and standardized processes to reduce errors and variability across sites.

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Case Study #1: Complex IV Frozen Product

Product Storage and Preparation

The investigational product is stored at -80°C and requires careful thawing before reconstitution.

Time-Sensitive Infusion Protocol

Infusion must start within four hours post-thaw and complete within eight hours, ensuring drug efficacy and safety.

Operational Complexity and Monitoring

Pharmacy, nursing, and research staff coordinate closely to monitor patients and document detailed infusion parameters.

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Case Study #2 : Limited-Supply Oral Product

Patient Medication Titration

Patients receive three dose levels to titrate to the maximum tolerated dose, requiring careful dose adjustment.

Long-Term Follow-Up

Patients return every six months for resupply, compliance review, and accountability reconciliation.

Inventory and Waste Management

Limited drug supply demands accurate forecasting and minimal waste to ensure availability throughout the study.

Patient Responsibility and Adherence

Patients bear greater responsibility for correct medication administration and adherence over extended periods.

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Highest Impact Issues: Case Study #1

Cold-Chain and Inventory Risks

Managing -80°C storage and strict post-reconstitution timing is critical to avoid drug spoilage and missed doses.

Drug Accountability and Monitoring

Precise documentation of infusion timing, rate, and dose completeness ensures patient safety and data integrity.

Maintaining Treatment Blinding

Preventing unblinding through consistent preparation and infusion practices is vital to clinical trial integrity.

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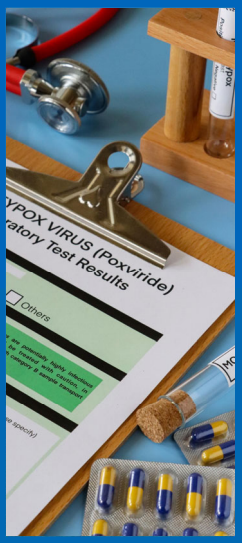
Highest Impact Issues: Case Study #2



Inventory Planning and Overage

Managing limited drug supply requires precise inventory planning and overage strategy to avoid trial disruptions.

Compliance Monitoring

Patient adherence monitoring through pill counts and self-reporting is critical for assessing drug efficacy.

Drug Accountability and Regulation

Reconciliation of returned medication ensures regulatory compliance and helps conserve drug supply.

Risk Profile Comparison

Comparing risk profiles between case studies highlights differences in inventory and compliance challenges.

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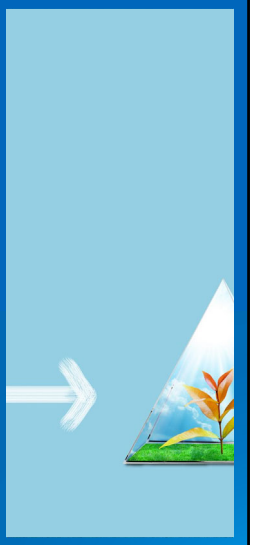
Impact if Issues Are Not Caught



Patient Safety Risks
Undetected issues can cause incorrect dosing, unmanaged adverse events, and exposure to mishandled drugs harming patients.

Data Integrity Compromise
Missing or inaccurate dosing records lead to unreliable data analyses and compromised study endpoints.

Operational Challenges
Sites face enrollment delays, protocol deviations, and staff burnout as problems accumulate without early detection.

Regulatory and Cost Consequences
Audit findings and oversight failures increase study costs and reduce sponsor confidence in the trial.

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How an Academic DCC Can Detect and Monitor Problems

Real-Time Integration
Integration of IWRS with EDC enables real-time tracking of randomization, dosing, and resupply triggers.

Risk-Based Monitoring
EDC risk-based monitoring identifies protocol deviations like out-of-window dosing or missing timestamps.

Centralized Cross-Site Analysis
Central monitoring enables detection of trends across multiple sites that individual sites might miss.

Pharmacy Monitoring
Unblinded pharmacy monitoring supports inventory reconciliation, preparation review, and cold-chain verification.

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Correction and Prevention Strategies

Preventive Measures
Robust SOPs, specialized training, and automated IWRS controls help prevent investigational product risks.

Inventory and Overage Strategies
Inventory buffers and clear overage plans reduce stockouts and waste, ensuring steady supply.

Issue Resolution and Retraining
Rapid deviation tracking and targeted retraining address root causes to prevent recurrence.

Data Reconciliation and Real-time Correction
Frequent reconciliation and real-time EDC data queries promptly correct documentation errors.

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Three Key Takeaways

System Integration Importance
Integration of IWRS, EDC, and pharmacy systems reduces manual errors and improves control over investigational products.

Focus on High-Risk Monitoring
Risk-based monitoring prioritizes resources on critical areas like cold-chain handling and long-term therapy compliance.

Value of Academic DCCs
Academic DCCs enhance study quality through centralized oversight, standardized processes, and data-driven decisions.

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Wrap up Slides

01	02	03	04	05
Standard of Care Variability	**Regulatory Compliance**	**Unexpected Issues in Surgery Trials**	**Complex Health Interventions**	**Investigational Product Tracking**
Sally Jo Zuspan *University of Utah*	**Michelle Lancet** *University of Pittsburgh*	**Bryan Blette** *Vanderbilt University*	**Brian Mittman** *Kaiser Permanente SC*	**Dixie Ecklund** *University of Iowa*
Unmanaged variation in standard of care affects eligibility, outcomes, and safety.	Electronic Master Regulatory Files automate compliance tracking and reduce the burden on both DCCs and sites.	Unexpected trial challenges can invalidate primary endpoints; pre-specify secondary measures as a safeguard.	Complex health interventions amplify trial challenges.	Investigational product accountability must be built into trial infrastructure from the start.

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Cross-Cutting Themes

1. **Assumption ≠ Reality**
   What looks clean on paper — standard of care, regulatory status, eligibility criteria, endpoint definitions — looks very different across real-world sites.
2. **Variability Is Inevitable; Unmanaged Variability Is the Problem**
   The goal is not to eliminate variation but to detect it, characterize it, and make deliberate choices about what must be controlled.
3. **Prevention Is Cheaper Than Correction**
   Pilot work, SOPs, eMRFs, fidelity monitoring, and pre-specification all cost less – in time, money, and credibility — than mid-trial amendments, FDA conversations, or endpoint switches.
4. **DCCs as Problem Anticipators, Not Just Problem Solvers**
   DCC's value is in asking 'what could go wrong?' before the trial starts, and building systems to catch drift early when it does.
5. **Documentation Is Protection**
   From video-certified gait assessments to eMRF alerts to fidelity logs for complex interventions — documentation protects participants, preserves data integrity, and shields studies from regulatory challenges.

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Questions

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