Should I Stay, or Should I Go? Results, Engagement, and End-of-Trial Decision Making

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Should I Stay or Should I Go?

Should I stay or should I go now?
Should I stay or should I go now?
If I go, there will be trouble
And if I stay it will be double
So come on and let me know

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Today's Agenda

- Background and significance: end-of-trial decision making
- Two case studies from concluded NIH Collaboratory-funded trials
- Methods
- Results: Emerging dimensions of the research problem
- Next steps
- Q&A

Background

- Locating our topic within the domain of embedded pragmatic clinical trials (ePCTs)
- Key questions for investigators and healthcare systems (HCS) to consider when trials end:
  - What happens when an intervention is shown to be ineffective?
  - What happens if an intervention is shown to be effective? What are the obligations?
  - What happens *before* the results are in?

❖**This last question is what we are exploring in this presentation and our current work**

A brief refresher on ePCTs

- Trials are set in routine health care ("embedded")
- Designed to show real-world effectiveness
- Broad eligibility criteria
- Use routinely collected electronic data
- Address clinically meaningful research questions
- Rely on critical partnerships between HCSs and researchers

(Ramsberg and Platt, 2017; Weinfurt et al., 2017)

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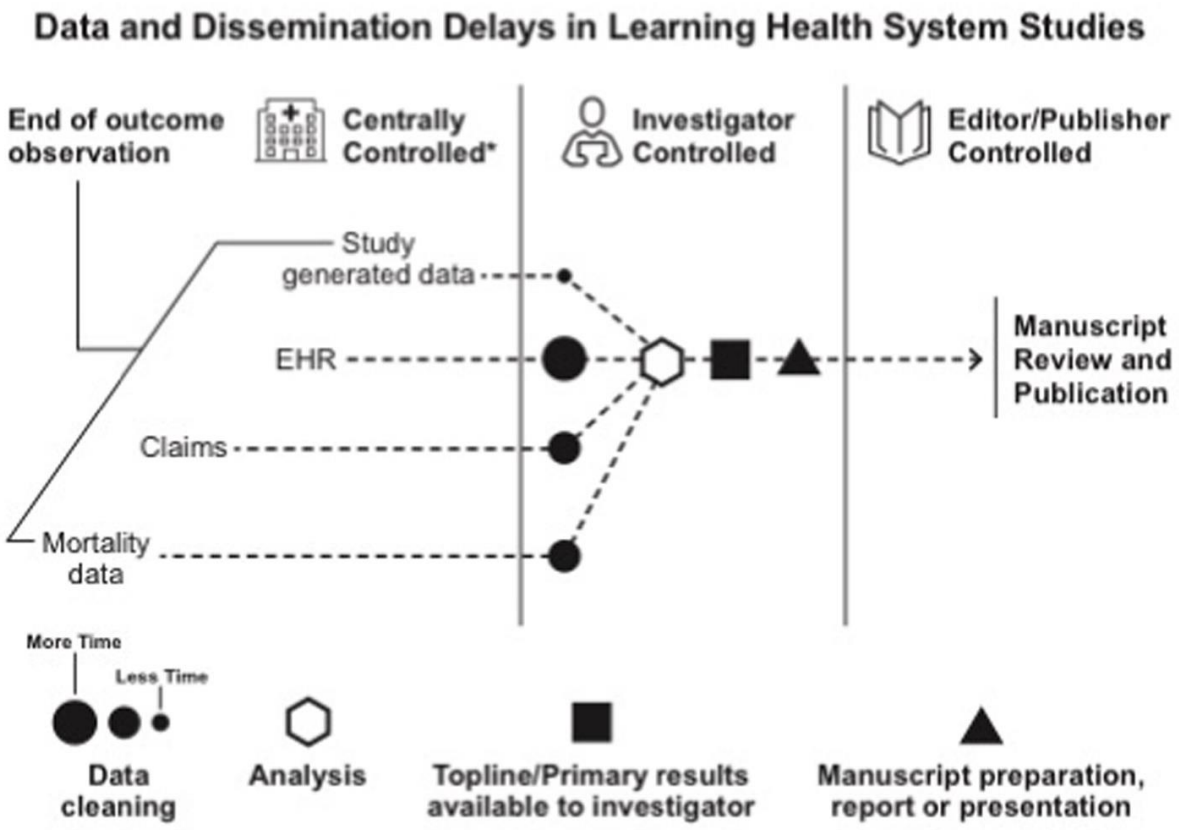
Data delays in ePCTs: An illustration



Simon GE, Richesson RL, Hernandez AF. Disseminating trial results: We can have both faster and better. Healthc (Amst). 2020 Dec;8(4):100474.

Why are delayed trial results significant?

- ePCTs often consider outcomes that take time to accumulate and use data that take time to arrive – the waiting period is often more than a year
- Decisions “while waiting” are often consequential, since either decision (continuing or stopping the intervention – “staying” or “going”) can take effort or resources to later reverse

Case study #1: Suicide Prevention Outreach Trial (SPOT)

- Objective: Compare 2 low-intensity outreach interventions with usual care for prevention of suicidal behavior among outpatients who report recent frequent suicidal thoughts
- Design and setting: Pragmatic, randomized clinical trial conducted at 4 US integrated healthcare systems
- Outcomes:
  - Primary: Time to first nonfatal or fatal self-harm event
  - Secondary:
    - More severe self-harm (leading to death or hospitalization)
    - Broader definition of self-harm (selected injuries and poisonings not originally coded as self-harm)

NIH Pragmatic Trials Collaboratory/Rethinking Clinical Trials, UH3 Project: Suicide Prevention Outreach Trial (SPOT)
https://rethinkingclinicaltrials.org/demonstration-projects/uh3-project-suicide-prevention-outreach-trial-spot/

Case study #1: Suicide Prevention Outreach Trial (SPOT)

- Decision while waiting for results: **Stop the interventions**
  - Overall considerations:
    - The interventions were resource intensive
    - Hope and expectation were that the interventions would be beneficial and would restart
    - Infrastructures and materials were preserved to work with the HCSs to resume the interventions if they proved effective

Case study #1: Suicide Prevention Outreach Trial (SPOT)

- Results: Negative trial
  - Lower percentage of fatal or nonfatal self-harm events for patient receiving usual care than for patients offered either of 2 trial interventions
    - Offering care management did not reduce outpatients' risk of self-harm compared to usual care.
    - Patients offered dialectical behavior therapy skills training had significantly greater risk of self-harm compared to usual care

Case study #2:Lumbar Imaging with Reporting of Epidemiology (LIRE)

- Objective: Evaluate the impact of including benchmark prevalence data in routine spinal imaging reports on subsequent spine-related healthcare utilization and opioid prescriptions
- Design and setting: Stepped-wedge, cluster randomized trial in 98 clinics across 4 large HCSs
- Outcomes:
  - Primary: 12-mo spine-related relative value units (RVUs)
  - Secondary:
    - Subsequent X-sectional imaging
    - Subsequent opioid prescriptions

NIH Pragmatic Trials Collaboratory/Rethinking Clinical Trials, UH3 Project: Lumbar Imaging with Reporting of Epidemiology (LIRE), https://rethinkingclinicaltrials.org/demonstration-projects/uh3-project-lumbar-imaging-with-reporting-of-epidemiology-lire/

Case study #2:Lumbar Imaging with Reporting of Epidemiology (LIRE)

- Decision while waiting for results: **It varied by site**
  - Site-specific considerations
    - Site A
      - The intervention was in place before the trial
      - No new resources needed to continue
      - No potential harms were anticipated
      - **Decision: Continue the intervention while waiting for results**
    - Site B
      - The intervention was not being done before the trial
      - New resources were needed to continue
      - **Decision: Discontinue the intervention while waiting for results**

Case study #2:Lumbar Imaging with Reporting of Epidemiology (LIRE)

- Site-specific considerations (cont.)
  - Site C
    - Significant new resources needed to continue the intervention with transition to a new EHR
    - **Decision: Discontinue the intervention and wait for results to see if benefits justify effort and cost**
  - Site D
    - No additional cost to continuing the intervention
    - Clinical stakeholders had positive reviews
    - **Decision: Continue the intervention while waiting for results**

Case study #2:Lumbar Imaging with Reporting of Epidemiology (LIRE)

- Results: Null trial
  - No reduction in spine-related health care utilization in the intervention group
  - Slight reduction in subsequent opioid prescription

Methods

- Reflections on case studies led to a broader inquiry
- In August 2022, the NIH Pragmatic Trials Collaboratory's HCSs Interactions Core convened 6 principal investigators of active ePCTs to explore decisions about maintaining or discontinuing interventions as studies end
- Meeting notes were thematically analyzed to surface dimensions and questions investigators should consider

Results

Six dimensions of maintenance vs. discontinuation of trial interventions

1. Ethical
2. Relational or political
3. Timing
4. Intervention specific
5. Resources
6. Trial design

Results

1. Ethical

- What effects (potential benefits or harms) could maintaining or not maintaining interventions have on continuing care of **trial participants**?
- What effects (potential benefits or harms) could maintaining intervention activities have on the care of **non-study patients** treated in trial settings?
- If true benefits and harms of study interventions are not known, how important are the perceptions of **health system partners** regarding benefits/harms?

Results

2. Relational or political

- How important is ongoing engagement with **health system partners** during period of waiting for study results? How might that affect future collaborations?
- What effects (potential benefits or harms) could maintaining or not maintaining intervention activities have on **system staff/providers**?

3. Timing

- How soon could investigators have a **preliminary assessment** of intervention benefits/harms? How long before a **definitive assessment**?

Results

4. Intervention specific

- To what degree have clinicians or other staff in participating health systems **adopted** intervention activities or practices **as standard work**?
- How much/how long are intervention activities or effects likely to **continue with no additional support** from the study team?
- What – if any – active **involvement of the study team** would be necessary to discontinue intervention activities?

Results

5. Resources

- What resources would be required to **maintain intervention** activities until results are known?
- What resources are available to **the study team** to support ongoing intervention delivery?
- What **intermediate options** (partial support requiring fewer resources) are possible?
- Will **health system partners** have adequate resources to take over intervention delivery if study results justify continuing?

Results

6. Trial design

- Have intervention activities been confined to only **some patients** (individually randomized trial), confined to **some units**, or **clusters** (cluster randomized trial), or spread to **all the participating health systems** (stepped-wedge trial)?
- How was maintenance of effects or effects of discontinuation addressed in the **original design**?

Next steps

- Refine this initial framework based on HCSs and researchers' experiences with ePCTs
- Test how dimensions and related considerations can be helpful to research teams and HCS stakeholders
- Explore implications of the questions we are raising for implementation, sustainment, and de-implementation of interventions

Q & A

THANK YOU!

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