Barriers, Challenges, and Lessons Learned from TiME

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TiME Trial Design

Enroll and Randomize Facilities

Intervention Facilities
≥4.25 hour sessions

Usual Care Facilities
(session duration not driven by trial)

Enroll and follow incident patients

Primary outcome:
All-cause mortality

Secondary outcomes:
Hospitalizations & Quality of Life

Follow-up: median 2.5 years
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<th>Barrier</th>
<th>Level of Difficulty</th>
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<td>Enrollment and engagement of patients/subjects</td>
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<td>Engagement of clinicians and Health Systems</td>
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<td>Data collection and merging datasets</td>
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<td>Implementing/Delivering Intervention Across Healthcare Organizations</td>
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Lesson:
People are less likely to opt out than to opt in.
Patient Enrollment

Mean Age, yr

**TiME** 64.0  **USRDS** 63.7  **HEMO** 55.8  **EVOLVE** 54.5
Lesson:
Difficult without either research staff on site OR health system staff who view themselves as part of the research team

- Active, ongoing interaction with clinicians and health system staff is critical – need systems for this
- Staff turnover, changing priorities need to be anticipated
Data Collection and Merging Datasets

Lessons:

• Collaborative approach between IT teams at DCC and health system is important during both trial planning and conduct

• Ongoing data review useful
Lesson:
There are many experts and many strongly held views -- do not be intimidated; conversations help.
Stability of Control Intervention

Lessons:

• Enthusiasm about the trial question can be a double-edged sword

• Stability of control intervention more likely if trial can be completed quickly
Stability of Control Intervention

• Lots of national attention to dialysis session duration
  – 4-hour treatments *almost* became a CMS clinical performance measure
  – New clinical practice guidelines include a maximum ultrafiltration rate (usually necessitates a longer session duration)

• We could not have dictated Usual Care session duration and still viewed trial as minimal risk
Implementing / Delivering Intervention Across Health Systems

Lessons:

• Not all interventions are the same
• Important to be able to track delivery of intervention
• Maybe a trial can be too pragmatic
PRECIS Scores

Johnson KE, Clinical Trials 2016
Most Important Lessons

• Progress is incremental
• Not all problems can be solved on the first try
• Celebrate successes, learn from challenges
  -- First trial conducted under true partnership between LDOs, academia, NIH
  -- Largest dialysis trial to date
  -- Navigated regulatory challenges for waiving consent in high risk patient population, mortality trial
  -- Use of single IRB for hundreds of sites
  -- TiME has generated tremendous interest in moving forward with this approach to evaluate other interventions in dialysis