Lessons Learned (so far) from the TiME Trial

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HCS Research Collaboratory
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If you come to a fork in the road, take it.
Lessons Learned

1. A highly developed and centralized health care delivery infrastructure does not obviate the need for activity at the local level and with individual practitioners and administrators.

2. What we view as a small change to work flow or IT system is often viewed by health system personnel as a large change.

3. There are many things we cannot control.

4. Not everything will work as initially planned.

5. Seemingly insurmountable problems usually have solutions.
**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:** 2-3 years
Eligibility Criteria

Facility
• Capacity to accommodate 4 hr, 15 minute treatments for incident patients
• Agreement by nephrologists and facility leadership to implement intervention

Patient
• Age >18 years
• Initiation of maintenance dialysis within past 120 days
• Ability to provide consent for dialysis care
Opt-Out Approach

• Patients are given a brief information document that includes
  – Purpose of the trial
  – How session duration will be affected by the trial
  – Toll-free telephone number to obtain additional information and to opt-out of participation

• Informational posters with research team contact information are posted in dialysis facilities throughout duration of the trial.
Sample Size and Power

• 402 facilities, 6432 patients
• Average cluster size: 16 patients
• 80% power for HR 0.85
Data Acquisition

• Clinical and administrative data are transmitted electronically from individual facilities and centralized laboratory to dialysis provider data warehouses (as in clinical care)

• De-identified data are transmitted from dialysis provider data warehouses to UPenn Data Coordinating Center
Pragmatic Features of the TiME Trial

• All patients starting dialysis are eligible unless they cannot provide consent to clinical care
• Intervention is delivered by clinicians
• Outcomes and all data elements are obtained through routine clinical care
• Adherence to intervention at the patient level is promoted using systems already in use
• Highly centralized implementation approach
• Single IRB of record
• Testing effectiveness rather than efficacy
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One Health Provider Organization = Thousands of Health Care Providers

• Buy-in and support from leadership is necessary but not sufficient

• Enrollment sites (400!) are made up of individuals with:
  – Different opinions
  – Different concerns
  – Different personalities
  – Different roles

• At facility level we need buy-in from:
  – Administrator
  – Medical Director
  – Every nephrologist
  – Patients
Small Changes to Us = Big Changes to Provider Organization and/or Facility

• Addition of 2 questions to CMS-mandated quality of life assessment

• Electronic documentation of eligibility and notification
We Cannot Control Everything

- Secular trend: longer dialysis
Not Everything Will Work as Initially Planned

• This should be expected and is okay.

• Example: change in approach to facility selection at one provider organization
“Insurmountable” Problems Usually Have Solutions

- CMS research tags for billing
- OHRP concerns
- FDA oversight

It is possible, and very helpful, to talk to individuals at these regulatory agencies
The TiME Trial is an Experiment

• Does longer session duration provide important benefits to patients?

• How can we conduct pragmatic clinical trials in the dialysis setting: what works and what doesn’t work?
TiME Trial Team

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- John Daugirdas – U Illinois
- Tom Greene – U Utah
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- Amy Young – DaVita
- Mary Burgess - DaVita
- Eduardo Lacson, Jr – Fresenius
- Christina Kahn – Fresenius
- Leland Brown - Fresenius

**NIDDK**
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- Denise Cifelli
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