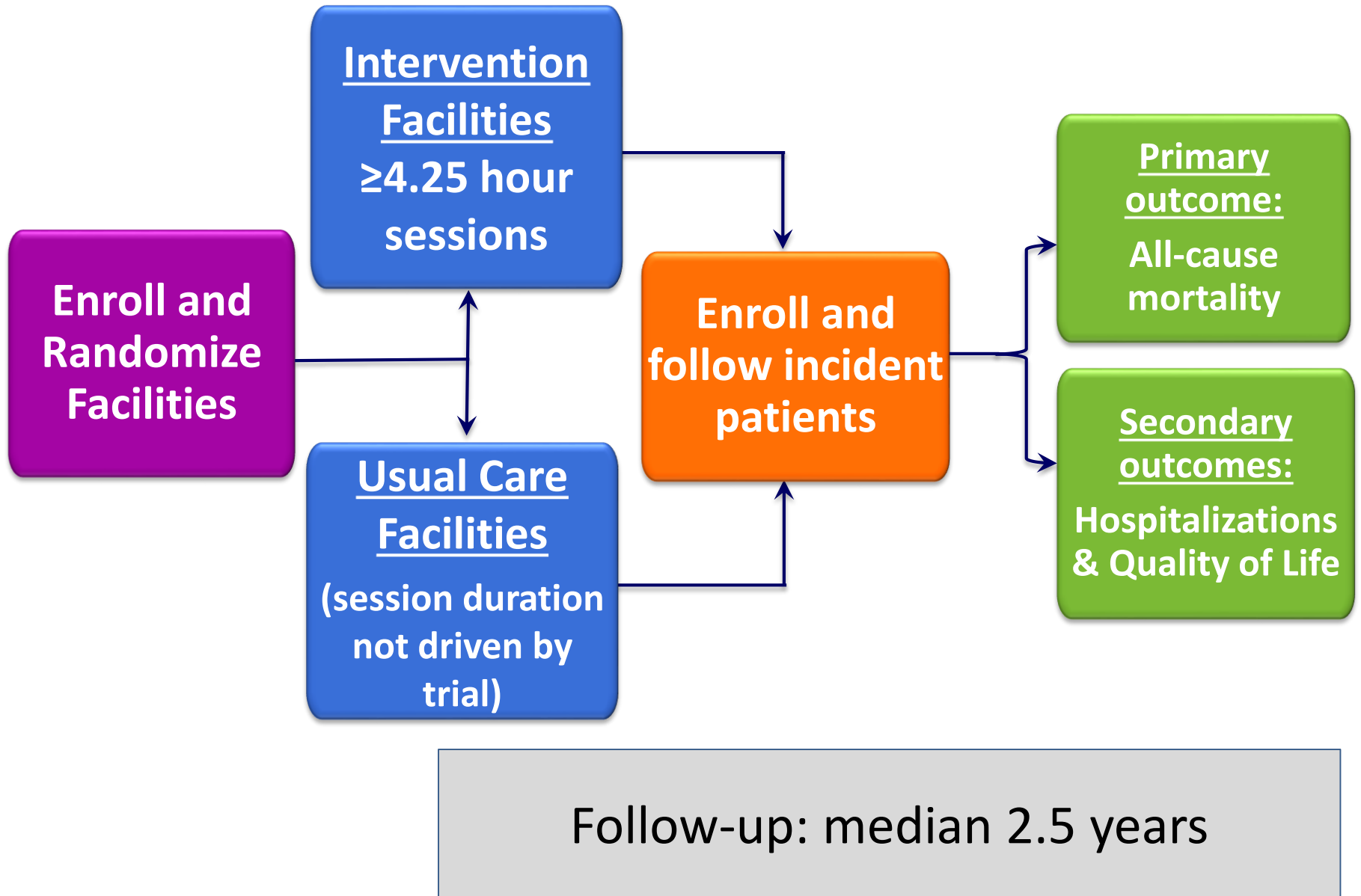


Barriers, Challenges, and Lessons Learned from TiME

Laura M. Dember, M.D.
NIH HCS Research Collaboratory
Steering Committee Meeting
May 23, 2017

TiME

TiME Trial Design



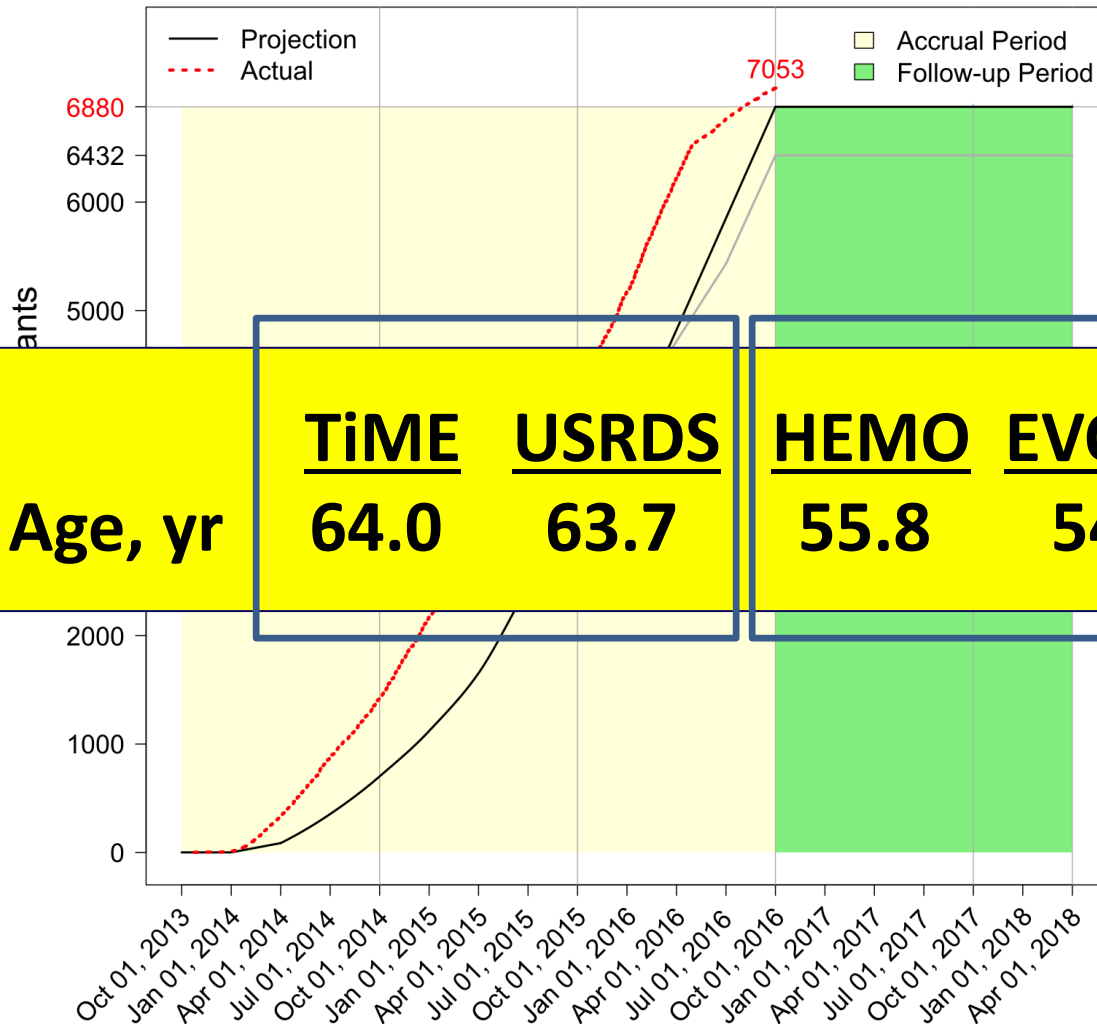
| Barrier | Level of Difficulty | | | | |
|--|---------------------|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 |
| Enrollment and engagement of patients/subjects | x | | | | |
| Engagement of clinicians and Health Systems | | | x | | |
| Data collection and merging datasets | x | | | | |
| Regulatory issues (IRBs and consent) | | x | | | |
| Stability of control intervention | | | x | | |
| Implementing/Delivering Intervention Across Healthcare Organizations | | | | | x |

Patient Enrollment

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

Patient and Clinician Engagement

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

Regulatory / IRB Issues

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

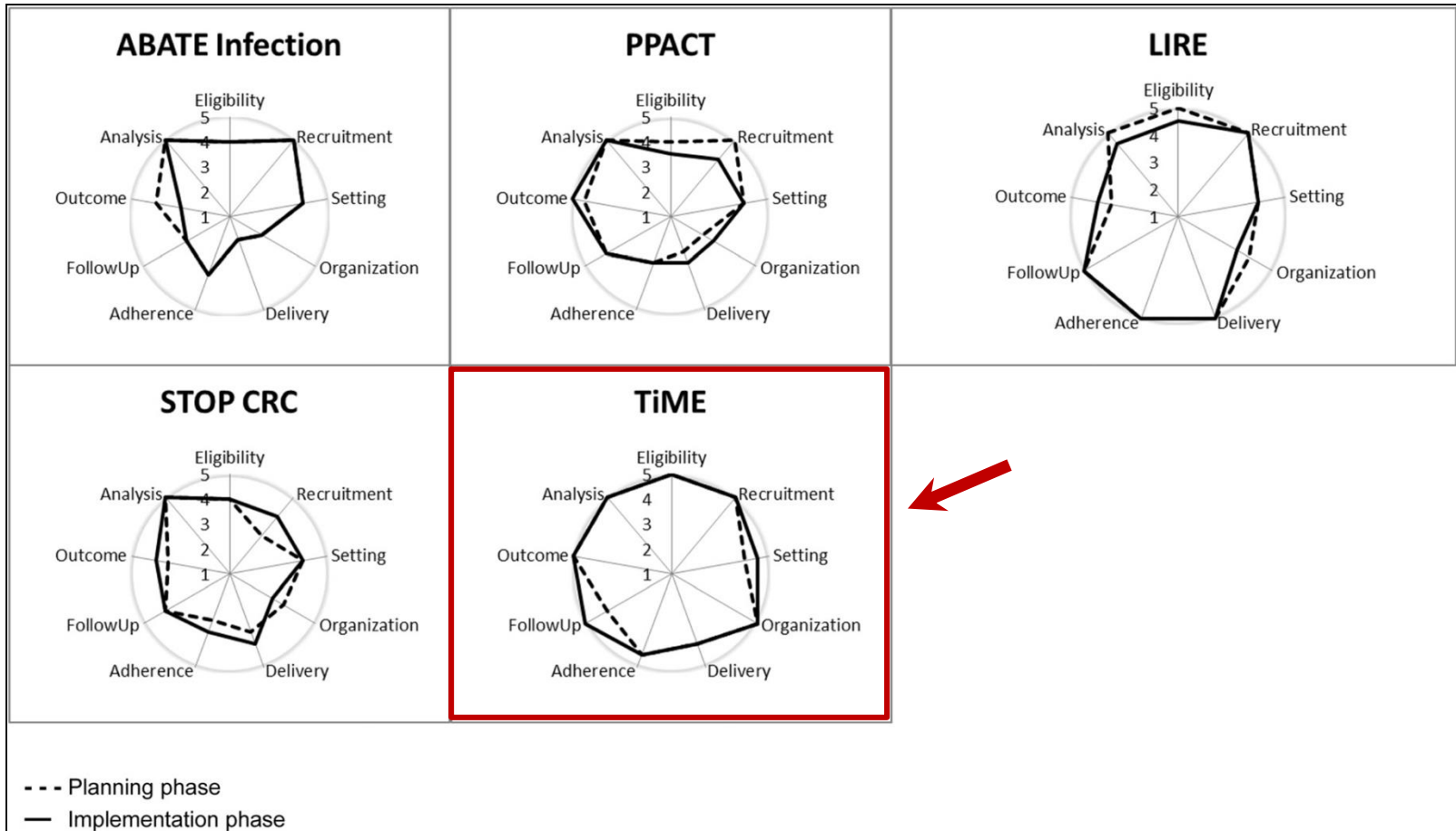
- Lots of national attention to dialysis session duration
 - 4-hour treatments *almost* became a CMS clinical performance measure
 - New clinical practice guidelines include a maximum ultrafiltration rate (usually necessitates a longer session duration)
- We could not have dictated Usual Care session 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



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