Lessons from TiME:
A Pragmatic Trial Demonstration Project

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CCEB

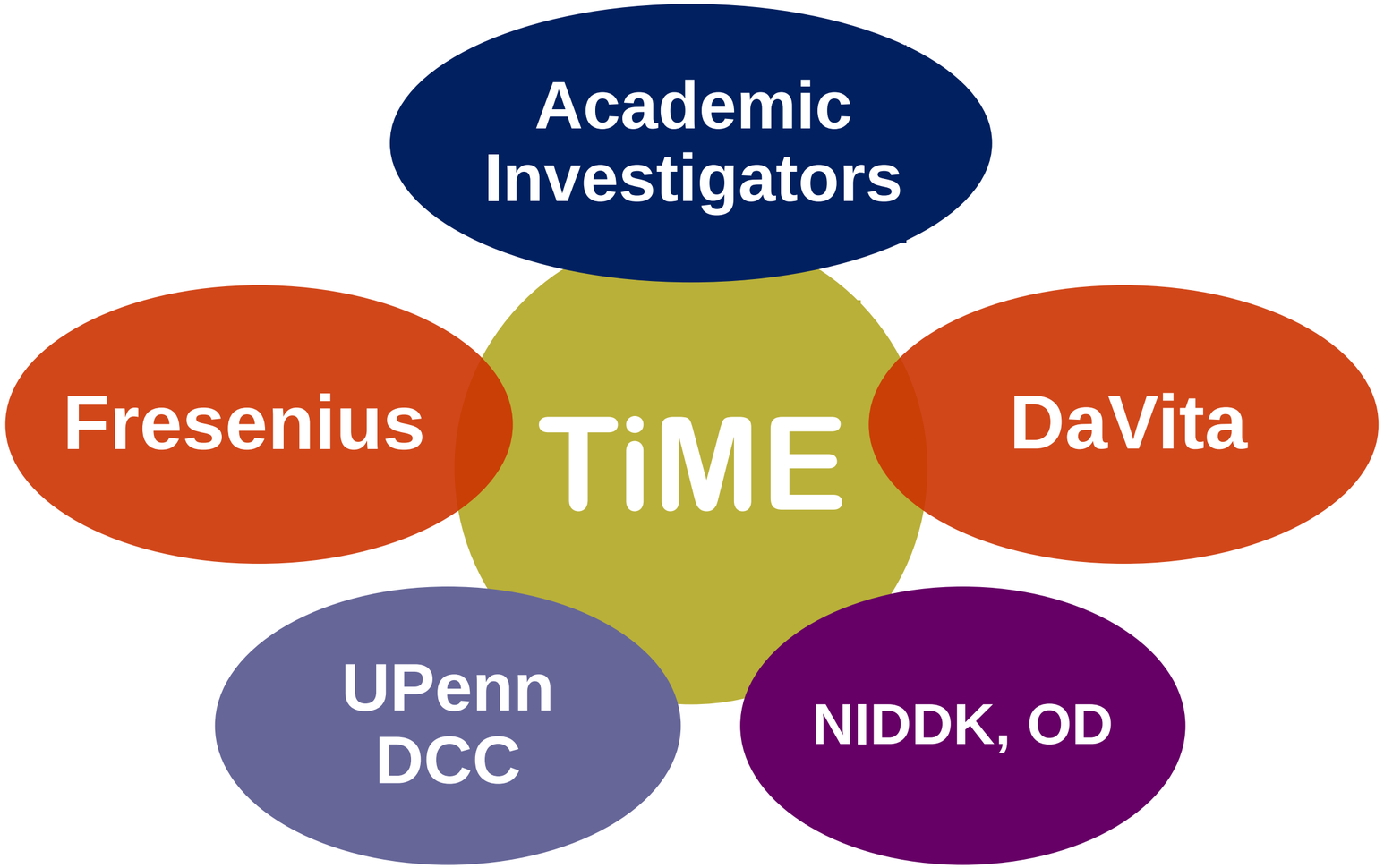
NIH Health Care Systems Research Collaboratory

Request for Applications 2012

- NIH initiative to advance pragmatic trials embedded in clinical care delivery
- Requirements
  - Conduct trial in partnership with ≥2 health care delivery organizations
  - Fully embed trial into clinical care delivery
  - Use hard clinical outcomes or patient reported outcomes
  - Ascertain outcomes from clinically available data

NIH Collaboratory Rethinking Clinical Trials®
Health Care Systems Research Collaboratory

Partners


Academic Investigators
Fresenius
TiME
DaVita
UPenn DCC
NIDDK, OD

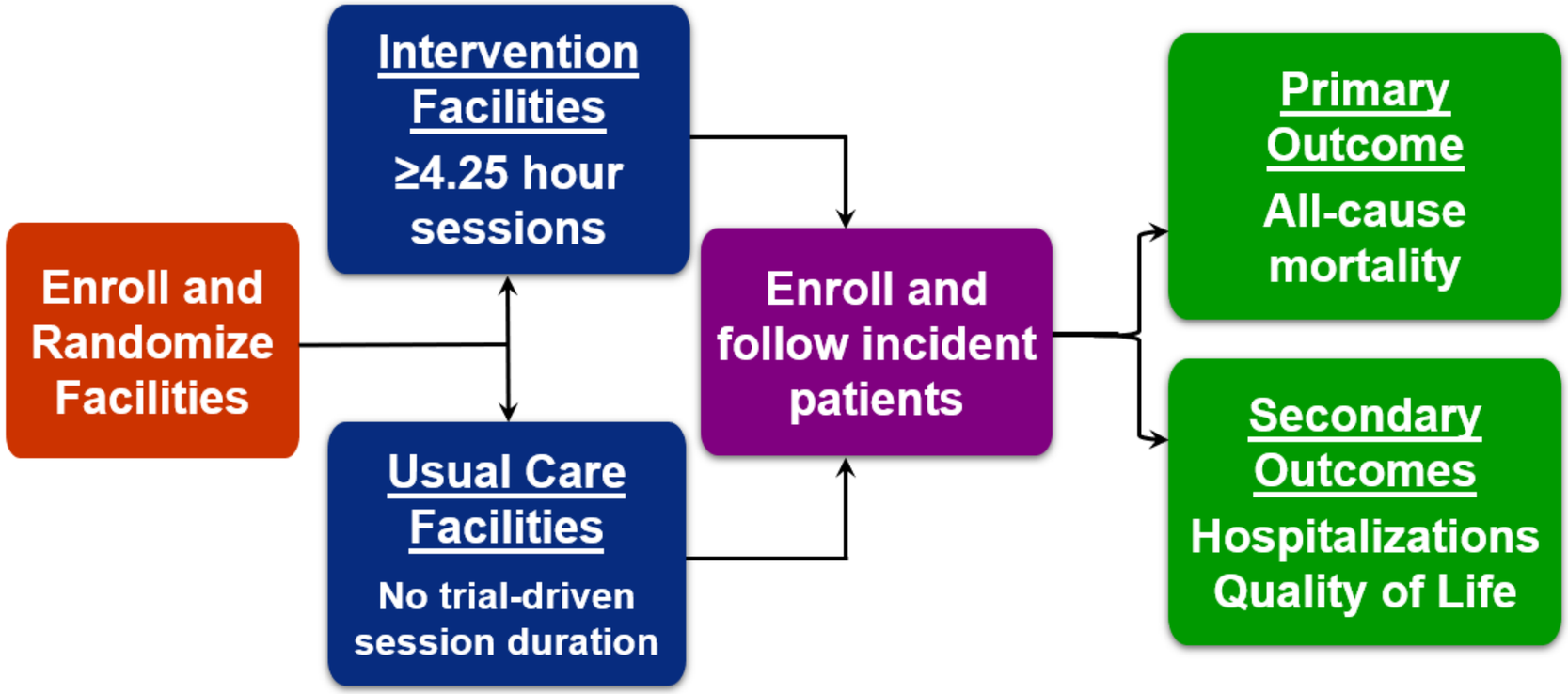
Trial Hypothesis

For thrice-weekly maintenance hemodialysis, treatment with session durations >4 hours will improve outcomes compared with usual care

Slower removal of fluid will result in:

- Less intra-dialytic hypotension
- Less myocardial “stunning”
- More consistent attainment of target weight

Design



- No on-site research staff
- No primary data collection for the trial
- Conducted under a waiver of consent

Eligibility Criteria

Facilities

- Willingness of nephrologists and facility leadership to adopt the 4.25 hour session duration for incident patients
- Capacity to accommodate 4.25 hour treatments

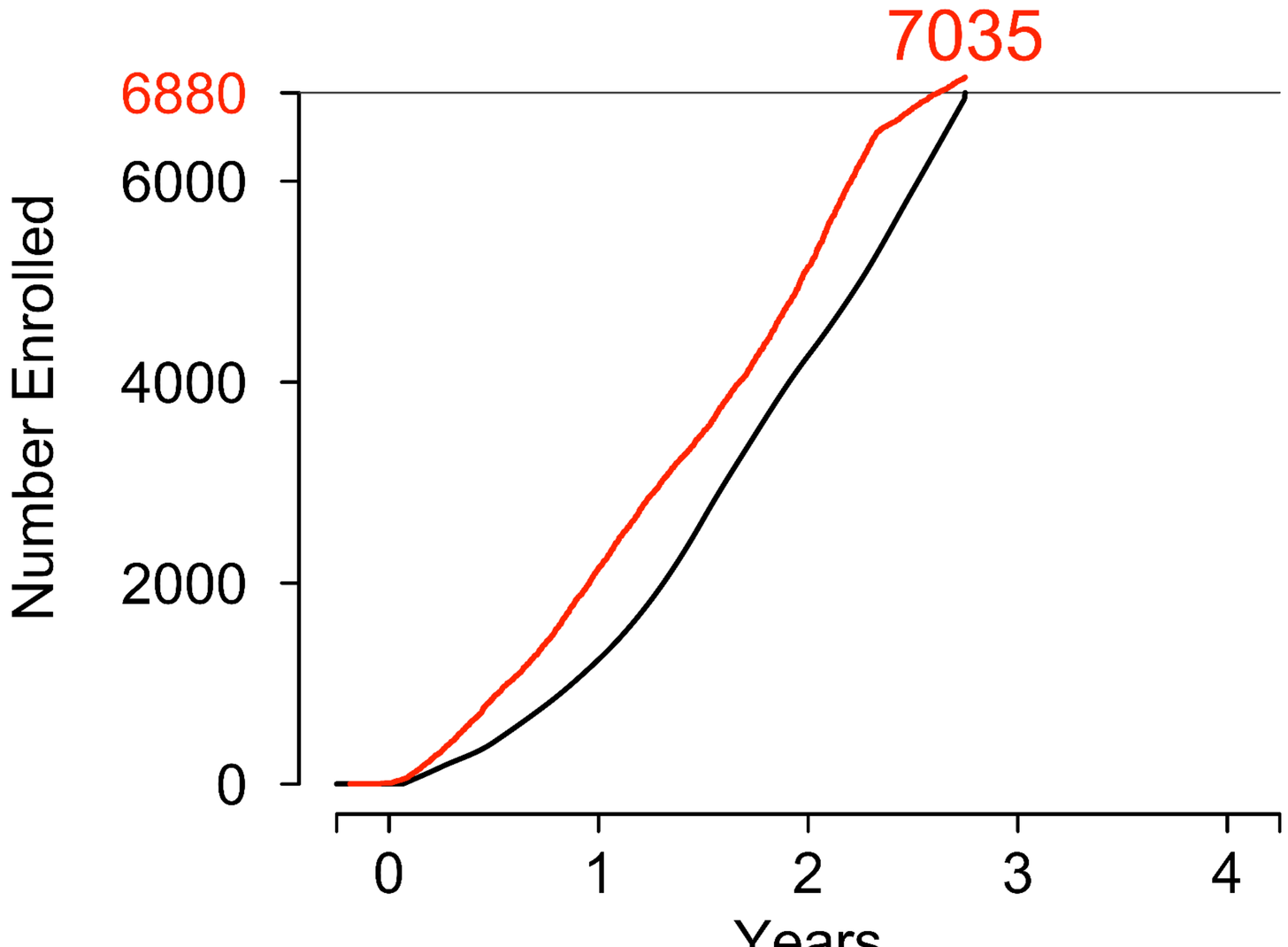
Patients

- Age >18 years
- Initiation of maintenance dialysis within 120 days
- Ability to provide consent for dialysis care

Engagement Activities

- Training webinars and conference calls prior to trial launch and during trial conduct
- Quarterly newsletters
- Monthly calls to discuss adherence
- Bi-monthly facility specific reports about adherence

Patient Enrollment



266 dialysis facilities

Baseline Characteristics

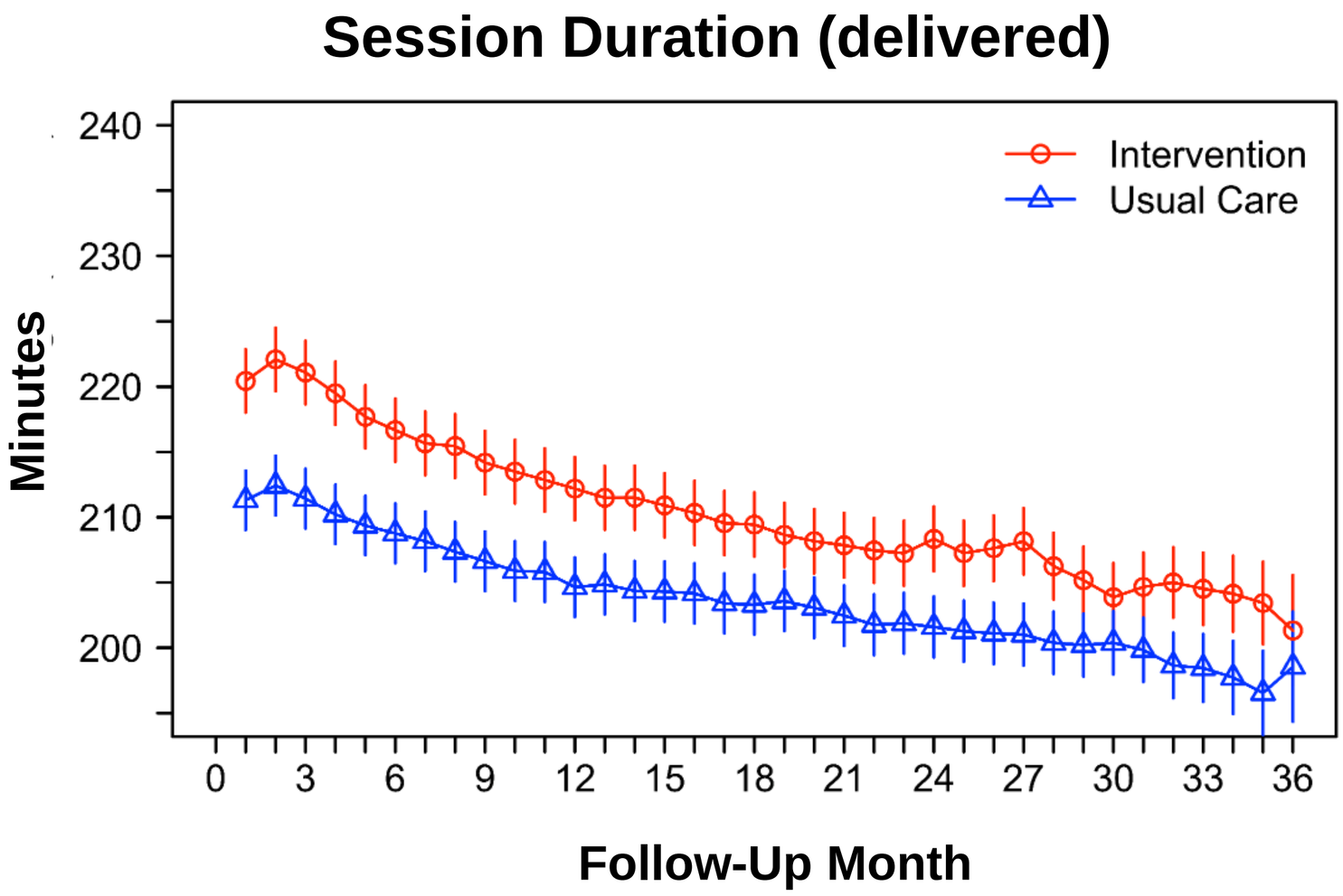
Charac	Full Analysis Population (N=7025)	
		l Care 3966)
Age, years		(14.7)
Male		(56.3)
Black		(24.8)
Hispanic		(11.2)
Weight, kg		(24.7)
Diabetes mellitus		(44.4)
Central venous catheter	2426 (79.5)	3219 (81.9)
Hemoglobi		
Albumin, g/		
Creatinine,		

	TiME	USRDS
Age, years	64.1	63.7
% Male	57.8	57.8
% Black	24.7	26.2
% Diabetes	44.0	43.9

	HEMO	EVOLVE	TiME	USRDS
Age	55.8	54.5	64.1	63.7

Dember LM et al. J Am Soc Nephrol; 30:890-903; 2019

Trial Terminated Early



Observations About Implementation

- Some dialysis units had outstanding adherence to the intervention
  - Nearly 100% of sessions for all participants throughout entire duration of trial were at target
- Facility was a major contributor to the overall variance in achieved target session duration
- Session duration decreased over time

Challenges for Intervention Implementation

- Required buy-in from all levels of health system
- Intervention was burdensome for patients
- Required uniform messaging from full clinical team
- Implementation affected by staff turnover
- Multiple health system initiatives competed for staff attention
- Clinicians were placed in a somewhat uncomfortable position

Conclusions

- Patients are willing to share their health data
- Clinical data from multiple dialysis providers is readily harmonizable
- Opt-out consent allows for efficient enrollment of trial cohort that is representative of overall dialysis patient population
- Effective approaches for engaging on-the-ground clinical care teams and patients are critical for interventions that are “palpable” to patients

What I Wish I Knew Then….

- Engagement, engagement, engagement!
- Clinician willingness to participate is not the same as buy-in and commitment
- Active, ongoing interaction with clinicians and health system personnel is critical but systems for interacting with clinicians are poorly developed
- Waiving consent can make it difficult to engage with patients