



NIH PRAGMATIC TRIALS COLLABORATORY

Rethinking Clinical Trials®

Time to Reduce Mortality in End-Stage Renal Disease (TiME)

Principal Investigator

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ClinicalTrials.gov Identifier

[NCT02019225](https://clinicaltrials.gov/ct2/show/study/NCT02019225)

Sponsoring Institution

University of Pennsylvania

Data and Resource Sharing

- [Data sharing checklist](#)
- Primary study results: Dember LM, Lacson E, Brunelli SM, et al. The TiME trial: a fully embedded, cluster-randomized, pragmatic trial of hemodialysis session duration. *J Am Soc Nephrol.* 2019;30(5):890-903. PMID: [31000566](https://pubmed.ncbi.nlm.nih.gov/31000566/).

Collaborators

- Fresenius Medical Care North America
- DaVita

NIH Institute Providing Oversight

[National Institute of Diabetes and Digestive and Kidney Diseases \(NIDDK\)](https://www.nidDK.nih.gov/)

ABSTRACT

Study Question and Significance: Although maintenance hemodialysis has been used for end-stage kidney disease for more than 50 years, there is uncertainty about the best approaches for many of the fundamental aspects of treatment, including the optimal duration of hemodialysis sessions. The objectives of the TiME trial were to evaluate the effects on mortality and hospitalization rates of hemodialysis session durations that are longer than many patients in the United States currently receive, and to establish approaches for embedding randomized clinical trials into the routine delivery of dialysis care.

Design and Setting: Cluster randomized trial conducted in 266 dialysis units operated by 2 large dialysis provider organizations. Dialysis units were randomized in a 1:1 ratio to either the intervention or usual care.

Intervention and Methods: Facilities randomized to the intervention adopted a default hemodialysis session duration of ≥ 4.25 hours, and facilities randomized to usual care had no trial-driven approach to session duration. Enrollment was restricted to patients new to dialysis (incident patients). The primary outcome was mortality, and the major secondary outcomes were hospitalization rate and quality of life. The trial relied entirely on clinical personnel and clinically acquired data.

Findings: The trial enrolled 7035 patients with demographic and clinical characteristics that matched those of the overall US hemodialysis patient population. The trial was discontinued after a median follow-up of 1.1 years because there was an insufficient difference in mean hemodialysis session duration between the intervention group and the usual care group. There was no reduction in mortality or hospitalization rate in the intervention group compared with usual care.

Conclusions and Relevance: Although the highly pragmatic design allowed efficient participant enrollment, data acquisition, and adherence monitoring, intervention uptake was insufficient to determine whether use of longer hemodialysis sessions improves outcomes. Effective approaches for engaging clinical personnel and patients are required to evaluate interventions fully embedded in care delivery.

GENERALIZABLE LESSONS

Challenge	Solution
Difficulty implementing the intervention, because there were no on-site research staff and the intervention was implemented by clinicians rather than researchers	Use of multiple approaches to engage facility personnel and participating patients during all stages of trial design and conduct
Incomplete ascertainment of a patient-reported outcome that was already being used routinely in clinical practice	Addition of processes to those already being used in clinical practice

“Buy-in from those ‘on the ground’ at the clinical sites, not just health system leaders, and effective engagement of clinicians and patients throughout the duration of the trial are important.” — Laura Dember

“If the trial includes a patient-reported outcome that is important for the analysis, concrete processes should be put in place ahead of time to maximize completion.” — Laura Dember

ADDITIONAL RESOURCES

- Article: [Patient and Physician Views about Protocolized Dialysis Treatment in Randomized Trials and Clinical Care](#)
- Article: [Willingness to Participate in Pragmatic Dialysis Trials: the Importance of Physician Decisional Autonomy and Consent Approach](#)
- Article: [Ethical Issues in Pragmatic Cluster-Randomized Trials in Dialysis Facilities](#)
- NIH Pragmatic Trials Collaboratory Steering Committee Meeting Presentation (2019): [TiME Trial: Challenges and Insights](#)

Access the complete set of [TiME resources](#).