NIH PRAGMATIC TRIALS COLLABORATORY

Rethinking Clinical Trials®

HiLo

A Pragmatic Trial Sponsored by the National Institutes of Health

Pragmatic Trial of Higher vs Lower Serum Phosphate Targets in Patients Undergoing Hemodialysis (HiLo)

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Sponsoring Institution
Duke University

Collaborators
- DaVita, Inc
- Dialysis Program, University of Utah Health

NIH Institute Providing Oversight
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ClinicalTrials.gov Identifier
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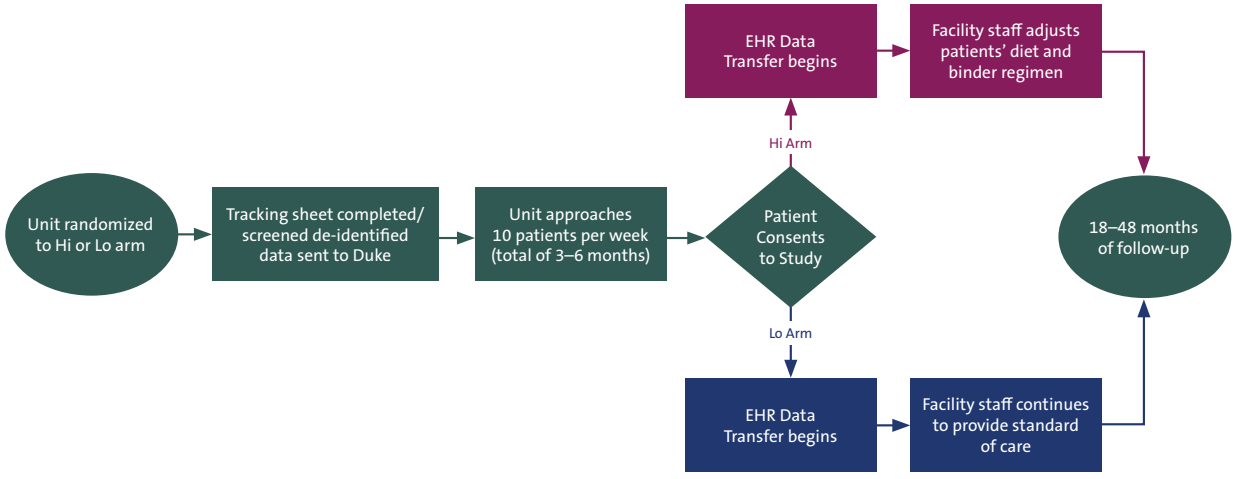
ABSTRACT

The prevalence of end-stage renal disease (ESRD) continues to increase. Kidney transplantation is the preferred treatment for ESRD, but an insufficient organ supply renders dialysis the only viable treatment option for most patients with ESRD. Although clinical outcomes among patients receiving dialysis have improved modestly in recent years, annual rates of hospitalizations and mortality remain unacceptably high, and quality of life is poor. Poor outcomes are driven primarily by increased risk of cardiovascular disease (CVD), but interventions that are proven to improve outcomes in the general population by targeting traditional CVD risk factors have mostly failed in patients with ESRD. In response, the nephrology community has embraced targeting of kidney-specific risk factors, including hyperphosphatemia, in an effort to improve clinical outcomes. Current clinical practice guidelines advocate aggressive treatment of hyperphosphatemia to near normal levels using dietary phosphate binders and restrictive diets. The benefits of this approach, however, are unproven, and the optimal serum phosphate target remains unknown and potential harms of aggressive treatment have not been definitively identified.

The HiLo Demonstration Project plans to address these clinically important questions in a large, pragmatic, cluster-randomized trial that will compare the effects of liberalizing the serum phosphate target ("Hi") versus maintaining aggressive phosphate control ("Lo") for patients receiving treatment with maintenance hemodialysis. HiLo will be embedded in the clinical care delivery of two U.S. dialysis organizations involving large and regional dialysis providers.



WHAT WE'VE LEARNED SO FAR

Challenge	Solution
Educating dialysis facility staff and patients around reevaluating current guidelines that call for aggressive lowering of serum phosphate levels.	Study team established a Patients Advisory Group of ambassadors to help convince providers and participants that the intervention is justified and important.
Developing and refining the use of a newer statistical approach to HiLo's primary hierarchical composite outcome of all-cause mortality and all-cause hospitalizations.	The lead statistician consulted with other statistical experts and has run numerous simulations, which have shown the approach to yield greater than 80% power in all instances.
Challenge of how to deploy an electronic process to obtain informed consent remotely—a first in U.S. dialysis studies—given that there will be no on-site study coordinators in the participating dialysis facilities.	Study team has developed a module using REDCap that will be loaded onto iPads that are shipped to the sites. Dietitians only need to pull up the patient profile in the module and hand the iPad to the patient, who will be guided through the consent process. The team has also established a voicemail system whereby patients can have questions answered by Duke nephrologists.

"The question at hand is something we grapple with on a daily basis in every dialysis facility across the country. Either answer will be important new information that will help us do a better job taking care of patients and hopefully improve their quality of life."

SELECTED PUBLICATIONS & PRESENTATIONS

- Presentation: Presentation to the NIH Pragmatic Trials Collaboratory Steering Committee (2023)
- Article (Study Design): Design and Rationale of HiLo: A Pragmatic, Randomized Trial of Phosphate Management for Patients Receiving Maintenance Hemodialysis (2021)

Access the complete set of HiLo resources.