VA | U.S. Department of Veterans Affairs

Establishing a Clinical Trials Platform to Support Pragmatic Trials for VHA Dialysis Patients

VA Boston Cooperative Studies Program

Overview

- Introduction & Lessons Learned from the Diuretic Comparison Project - Dr. Leatherman
- Dialysis Platform (DiaP): Overview & Inaugural Study, Beta Blocker Dialyzability on Cardiovascular Outcomes (BRAVO) - Dr. Ishani
- Patient Engagement & Advocacy - Mr. Hickey
- Facility & Provider Engagement - Dr. Kaufman
- Dissemination and Incorporating Results into Clinical Practice & Keys to Success - Dr. Kaufman
- Audience Questions

INTRODUCTION AND LESSONS LEARNED FROM THE DIURETIC COMPARISON PROJECT

Sarah Leatherman, PhD
Deputy Center Director
VA Boston Cooperative Studies Program Coordinating Center

VA | U.S. Department of Veterans Affairs

Disclosures

- None

The Problem

- Healthcare system's information needs are not met by the current research enterprise
  - Designed for basic science inquiry and drug biomarker discovery
  - Asynchronous worlds
  - Scalability

A Solution:

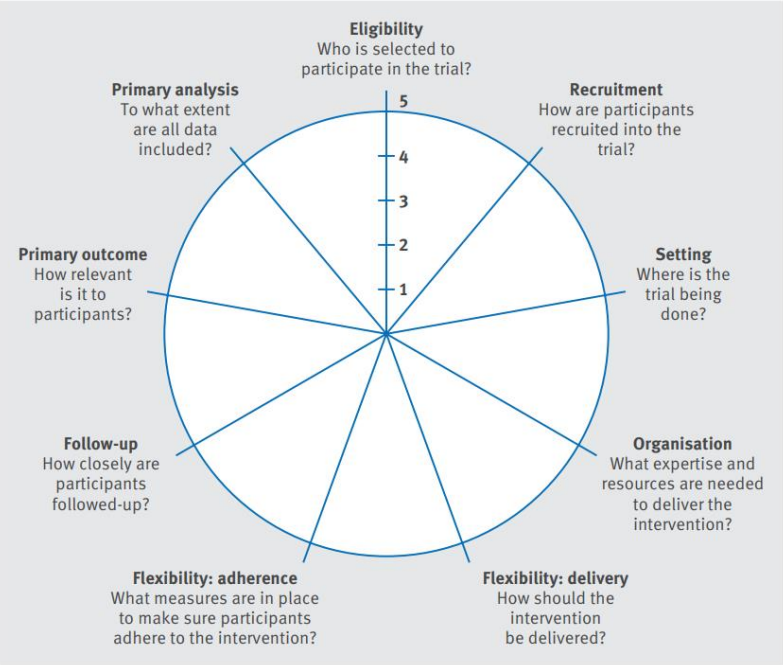
- Creation of a learning healthcare system that creates locally applicable knowledge
  - Identifies its own needs
  - Uses its own infrastructure
  - Uses available research methodologies and expertise
  - Directly implements research results into practice

- The knowledge gained is not generalizable (thus, not “research”), but rather is locally selfish.

VA Point-of-Care Research

- Trials embed research into clinical care
- Minimal disruption to clinical workflow
- Minimal burden for patients
- Reduce research infrastructure and costs
- Use of real world data (RWD) for all study processes

Pragmatic Clinical Trials



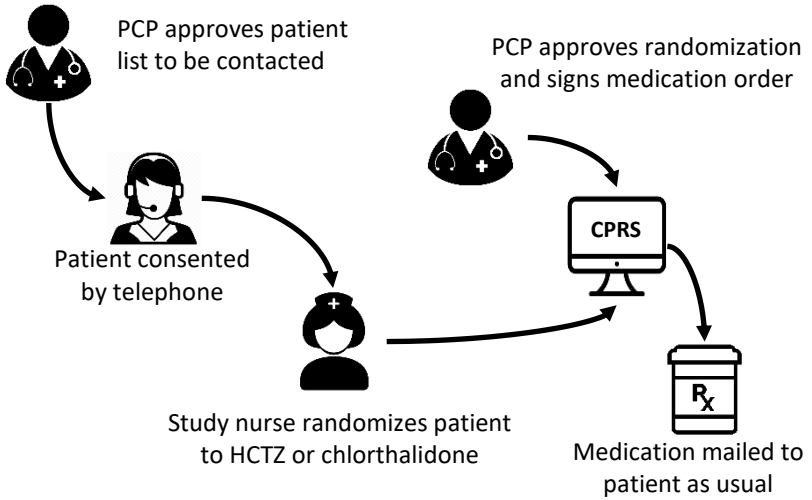
The PRagmatic-Explanatory Continuum Indicator Summary 2 (PRECIS-2) wheel.

- Level of risk to patients
- Clinical workflow
- Availability of data

Loudon, et al. The PRECIS-2 tool: designing trials that are fit for purpose. *BMJ*. 2015.

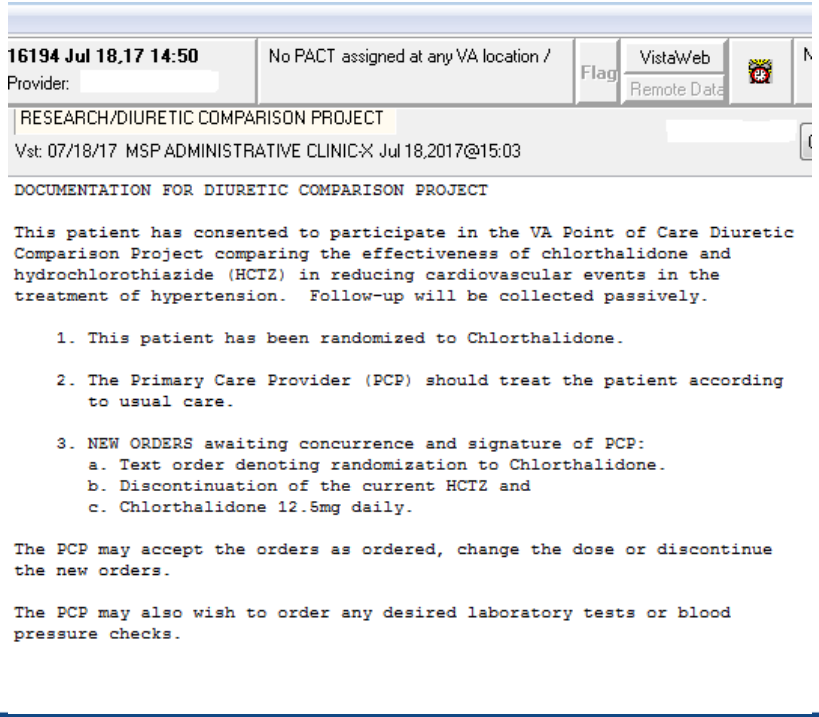
Case Study

- The Diuretic Comparison Project (DCP) was designed to compare hydrochlorothiazide and chlorthalidone on MACE outcomes.
- After randomization, PCPs provided usual care to patients without follow-up study visits, labs, phone calls, etc.
- Enrolled at 72 healthcare facilities (representing 500+ clinics). Randomized 13,523 patients and consented 4,200+ providers.



Key Features

- Telephone informed consent
- Randomization through EHR
- Usual care follow-up
- Data collected through EHR and Medicare

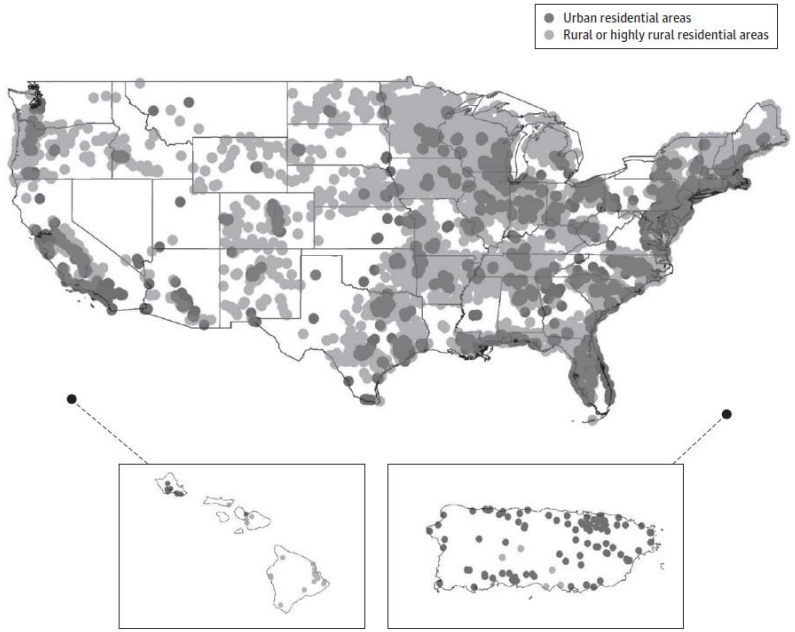


What We've Learned

- Expanded reach of potential subjects
- No free lunch (free data is work!)
- Potential for improved enrollment
- Low impact on providers

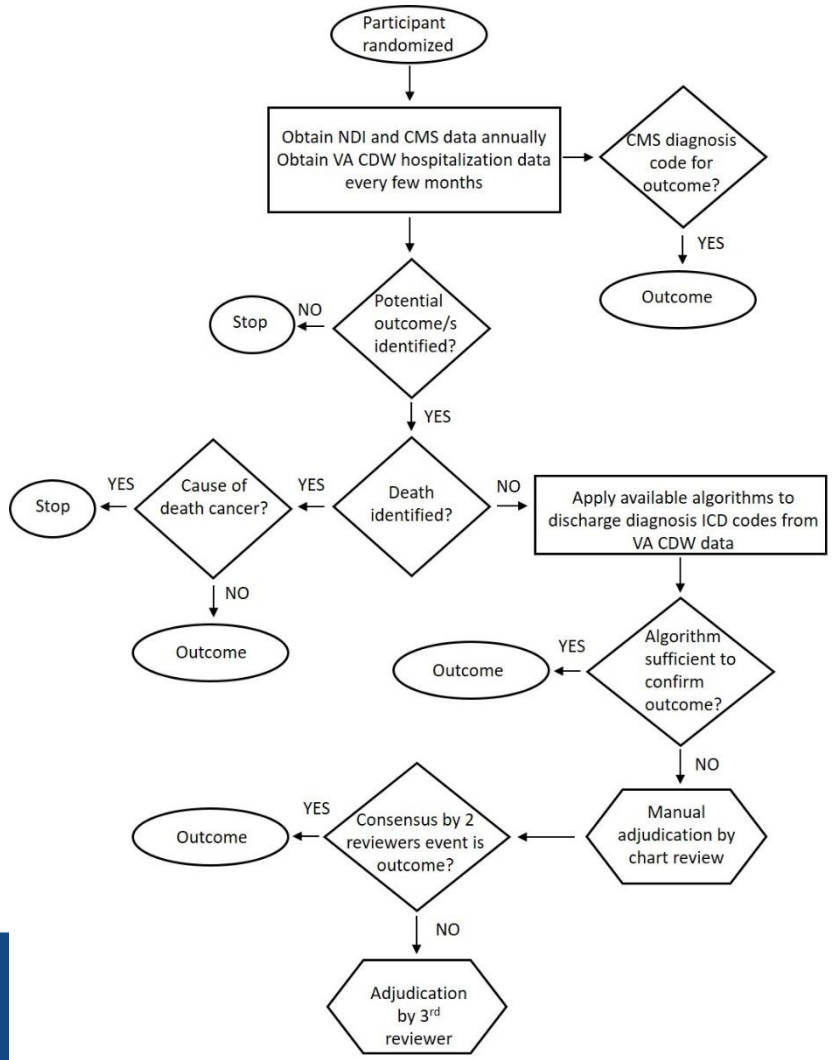
Expanded Patient Reach

Figure 3. Geographic Distribution of Randomized Patients Across the US



Residential locations of 13 523 included patients were graphically rendered using the geographic information system data extracted from the VA Cooperative Data Warehouse (CDW). The CDW is a centralized repository to combine and store EHR data generated from all VA health care facilities. Dots correspond to participants residing in urban (dark shading) vs rural and highly rural (light shading) locations, but respectively do not infer density.

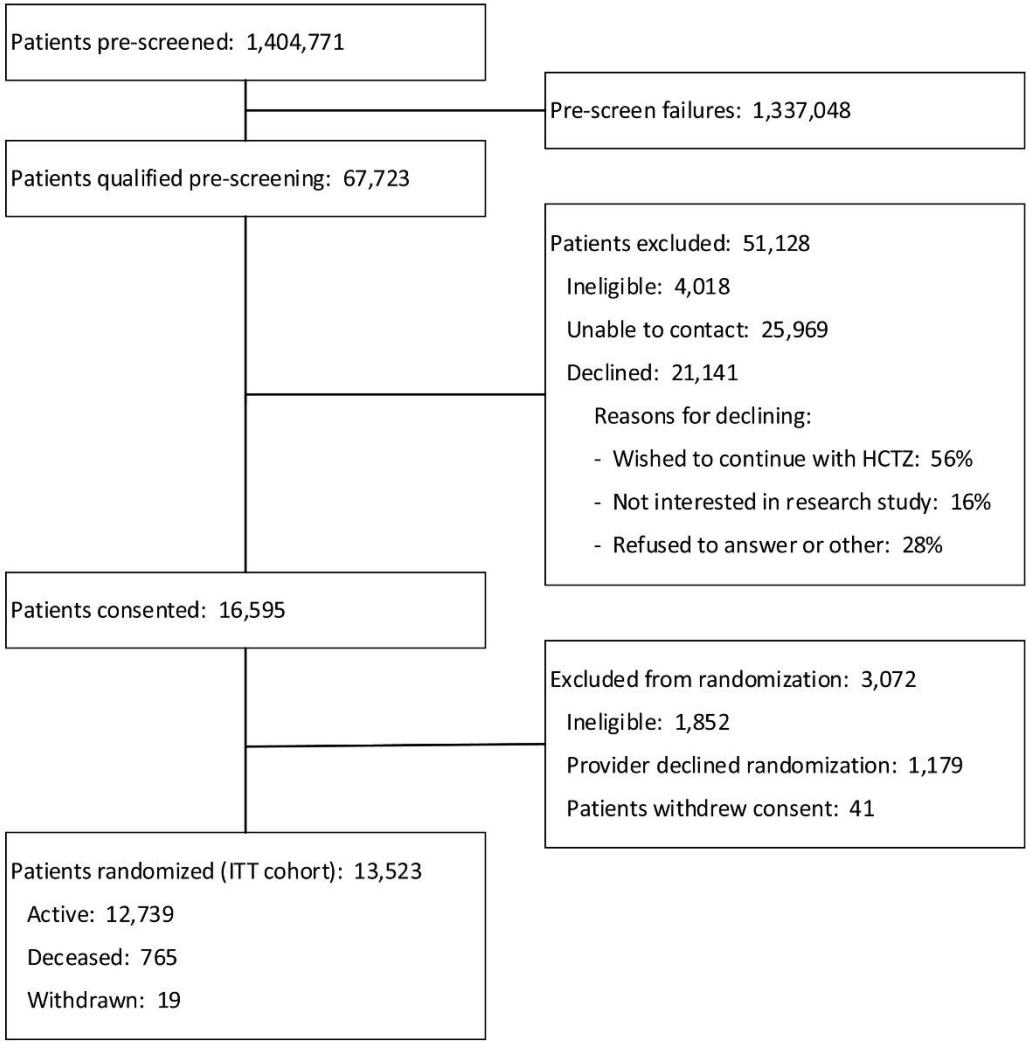
Hau C, Efird JT, Leatherman SM, et al. A Centralized EHR-Based Model for the Recruitment of Rural and Lower Socioeconomic Participants in Pragmatic Trials: A Secondary Analysis of the Diuretic Comparison Project. *JAMA Netw Open.* 2023;6(9):e2332049. doi:10.1001/jamanetworkopen.2023.32049



Free Data is Work

- No free lunch
- Accept there will be error
- Validation
- Reusable!

b)



Efficient Enrollment

- Quick screening
- High recruitment rate
- Low dropout and withdrawal

Ishani A, Leatherman SM, Woods P, Hau C, Klint A, Lew RA, Taylor AA, Glassman PA, Brophy MT, Fiore LD, Ferguson RE, Cushman WC. Design of a pragmatic clinical trial embedded in the Electronic Health Record: The VA's Diuretic Comparison Project. Contemp Clin Trials. 2022 May;116:106754. doi: 10.1016/j.cct.2022.106754. Epub 2022 Apr 4. PMID: 35390512.

Providers Like It

"I am a busy clinician. Having a pragmatic RCT that minimizes the burden on the PCP is important in this day and age."

"I liked that it was easy to implement and was a comparison of similar drugs so some patients were not getting inferior care with this model."

"This study did not affect regular patient care and management did not change as a result of the study. This is was very important to me as a provider. "

"Excellent job. Happy to participate. Minimal to no time required by PCPs is the key. "

CONTINUED CHALLENGES

Engagement

- Patients
- Providers
- Leadership
- Payers

Regulatory

- Resistance from IRBs
- Acceptance by FDA

Real World Data

- Combining data sources
- Availability of critical data
- Timeliness

VA DIALYSIS PLATFORM (DIAP): OVERVIEW & INAUGURAL STUDY, BETA BLOCKER DIALYZABILITY ON CARDIOVASCULAR OUTCOMES (BRAVO)

Areef Ishani, MD MS
Principal Investigator, CSP 2026 DiaP & BRAVO
Director Primary Care and Specialty Care ICC Minneapolis VAHCS
Director Specialty Care ICC VISN 23
Vice Chair and Professor, Department of Medicine, University of Minnesota

VA | U.S. Department of Veterans Affairs

Disclosures

- None

Dialysis and Outcomes

- Dialysis is more common in the veteran population compared to the general population
- Patients on dialysis have an increased risk of cardiovascular outcomes, poor quality of life and a very high mortality rate
- Dialysis is also very expensive for health care plan
- Few studies are conducted in patients on dialysis – so there are very few interventions that are known to improve outcomes

Dialysis Platform (DiaP)

- The Dialysis Platform (DiaP) will provide an infrastructure to support sequential and concurrent randomized clinical trials relevant to the VA dialysis population with a primary focus on comparative effectiveness trials.
- DiaP will include a prospective registry of all VA dialysis patients (facility and CITC)
  - Prevalent and incident patients
  - and who have a primary care provider at the VA and receive their medications at the VA

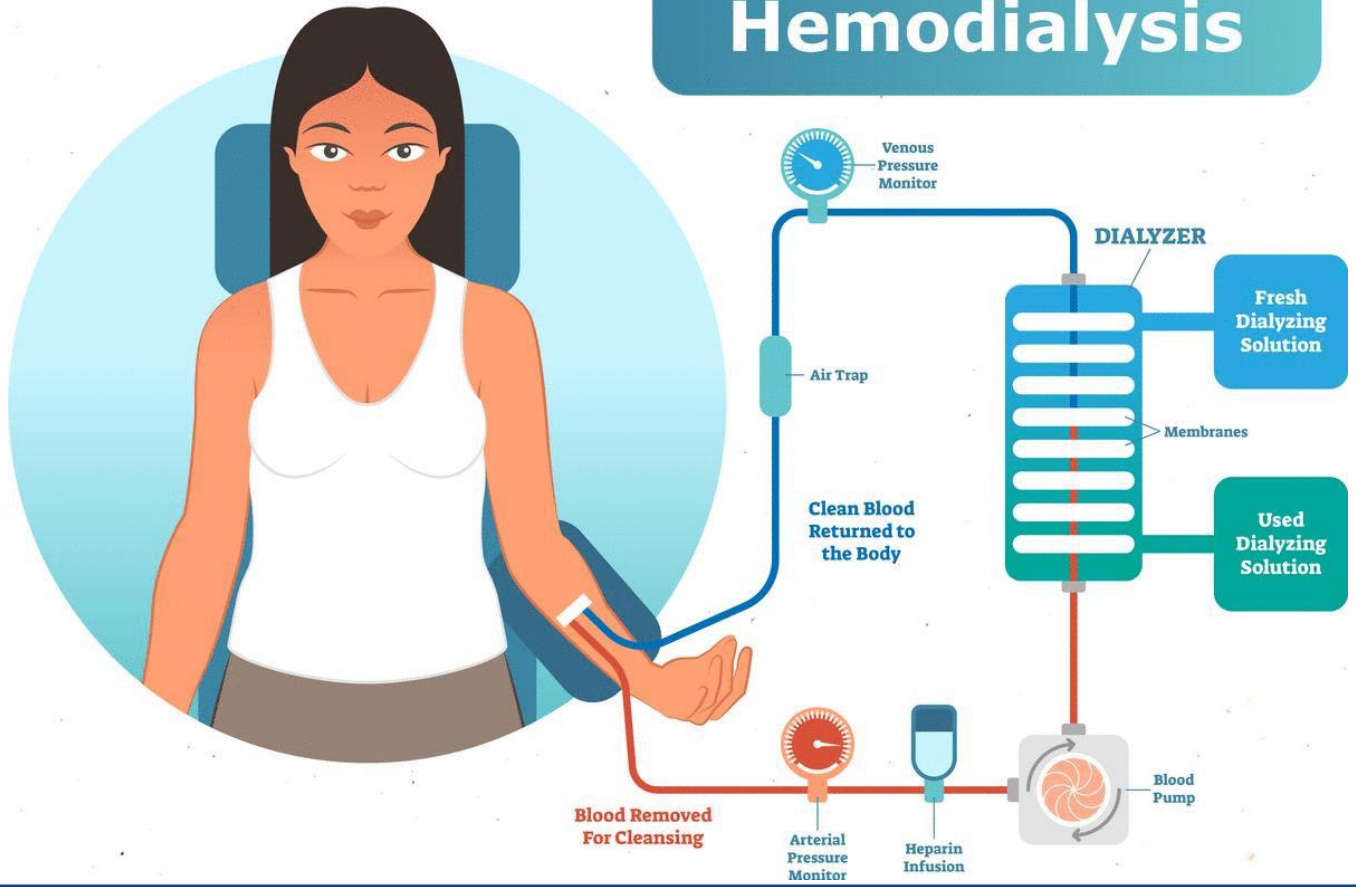
Dialysis Platform (DiaP)

- Platform for interested investigators to submit projects for review and implementation, to identify and enroll potential participants, collect necessary trial data, and assist in data analysis and manuscript preparation
- The executive committee of the platform is a resource to vet potential trials and to ultimately help get them funded and implemented

Beta Blocker Dialyzability on Cardiovascular Outcomes (BRAVO)

- The goal of dialysis to remove toxins from the body
- Some drugs are removed during the dialysis session while others are not

Hemodialysis

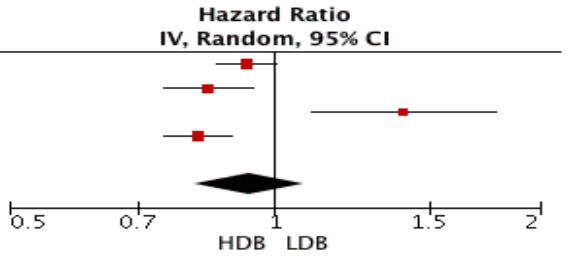


Why do the study?

All-cause Mortality - hazard ratios

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
Assimon	−0.0726	0.0399	29.0%	0.93 [0.86, 1.01]
Shireman	−0.1744	0.0598	26.1%	0.84 [0.75, 0.94]
Weir	0.3365	0.123	16.6%	1.40 [1.10, 1.78]
Wu	−0.1985	0.0455	28.3%	0.82 [0.75, 0.90]
Total (95% CI)			**100.0%**	**0.94 [0.81, 1.08]**

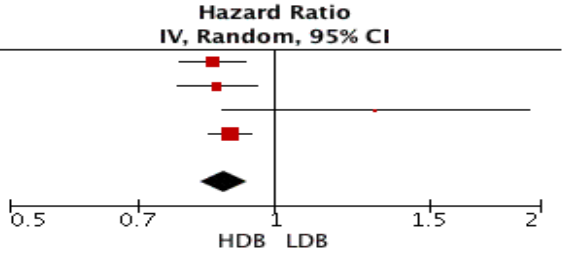
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 18.96$, df = 3 (P = 0.0003); $I^2 = 84\%$
Test for overall effect: Z = 0.93 (P = 0.35)



Cardiovascular Events - hazard ratios

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
Assimon	−0.1625	0.0438	30.0%	0.85 [0.78, 0.93]
Shireman	−0.1508	0.0531	23.4%	0.86 [0.78, 0.95]
Weir	0.2624	0.2047	2.2%	1.30 [0.87, 1.94]
Wu	−0.1165	0.0295	44.4%	0.89 [0.84, 0.94]
Total (95% CI)			**100.0%**	**0.88 [0.83, 0.93]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 4.59$, df = 3 (P = 0.20); $I^2 = 35\%$
Test for overall effect: Z = 4.17 (P < 0.0001)



Tella, Abhinav, William Vang, Eustacia Ikeri, Olivia Taylor, Alicia Zhang, Megan Mazanec, Srihari Raju, and Areef Ishani. 2022. “β-Blocker Use and Cardiovascular Outcomes in Hemodialysis: A Systematic Review.” *Kidney Medicine* 4 (5): 100460.

Recruitment

- Hybrid
- 20 sites will have study coordinators
  - Will be similar to the VISN model – home site and will travel to nearby VA dialysis units to recruit and consent patients
  - Will also recruit CITC dialysis patients from their assigned sites
- Centralized recruiters
  - Call patients at remote VA sites
  - Recruit patients enrolled in the CITC dialysis program

- Minneapolis/VISN23 will be the inaugural site

Consent

- Inclusion: Veteran on dialysis at a VA site or through the CITC program who is getting a beta blocker from the VA with a VA prescriber
- Consent will occur by phone
- Waiver of documentation of informed consent
  - Study is minimal risk

Consent

- Study will only include dialysis patients currently taking a beta blocker
- Beta blockers are a class of blood pressure drugs that are commonly used in dialysis patients (60-70% of the patients)
  - At initiation of the study approximately 50% of VA dialysis patients are taking metoprolol and about 50% are taking carvedilol
  - Randomization will keep individuals on currently established medications
    - Previous pharmacy drug shortages have routinely switched patients back and forth between metoprolol and carvedilol – without notification to prescribers

Logistics

- Patient randomized to metoprolol succinate or carvedilol
  - Filled through the VA pharmacy as usual care (not research medication, not blinded)
- After randomization – everything is considered usual care – up to the veteran's team

Events

- Event Driven: 1,100 events over 4.5 years
  - Assumes a 20% yearly event rate in the metoprolol arm and 16.25% yearly event rate in the carvedilol group
  - 90% power and 1 interim analysis

Outcomes

- Primary endpoint
  - Time to the composite end point of death, non-fatal myocardial infarction, stroke or heart failure hospitalization
- Secondary endpoint
  - Time to the first occurrence each of death, non-fatal myocardial infarction, stroke or heart failure
- Tertiary/Safety endpoint
  - ED visit or hospitalization related to low BP – including falls, fractures, hypotension or serious injury
  - Use of BP raising medications (midodrine)
  - ED or hospital visits for atrial fibrillation and uncontrolled rate
  - Intra-dialytic hypotension

Conclusion

- Platform and the first comparative effectiveness study in dialysis patients in the VA
- Leveraging the pragmatic concept in the VA – with many similar traits to the DCP study

DEFINING THE VALUE OF PATIENT ENGAGEMENT

A PATIENT ADVOCACY ORGANIZATIONAL PERSPECTIVE

Edward Hickey III, JD
President, American Association of Kidney Patients (AAKP)
Chair, AAKP Veterans Health Initiative, U.S.M.C.

VA | U.S. Department of Veterans Affairs

Disclosures

- None

AAKP Overview

Who we are…

The American Association of Kidney Patients (AAKP) is the oldest and largest kidney patient education and advocacy organization in the nation. AAKP proudly represents the largest base of patient consumers, families, organ donors, and care partners in the kidney space.

What we do…

Founded in 1969 by six kidney patients, AAKP has always been a patient-led organization. We educate patients and policymakers on the need for greater investments and innovations in kidney disease research, detection, and treatment. We are known nationwide and across the globe for our aggressive advocacy on behalf of kidney patient consumers and **their right to treatment care choice**, in consultation with the doctors who **they** choose to care for them.

We believe…

AAKP defines high-quality kidney care as timely patient access, without interference, to innovations that help prevent and treat diseases, and empower patients to remain healthy, independent, and better able to pursue their aspirations - including meaningful full-time or part-time work and a career; home ownership; starting and supporting a family; and a secure retirement.

Partnering with Patients

- <u>Short term efforts lead to long term benefits</u>
  - You may “know” your market, but do you “understand” your market?
  - Co-development approach to study design, clinical trial site selection, clinical trial materials, clinical trial recruitment efforts.
  - All these early efforts will support a higher degree of patient satisfaction, increased levels of support and enthusiasm for innovation, and cultivate a stronger relationship between patients and companies/researchers.

The Power of Patient Organizations

Center for Patient Engagement & Advocacy

Engagement

- **Ambassador Initiative** (National/International/Veterans/Military Families)
- **Ambassador Toolkit/Handbook**
- **Ambassador Certification Program - in development**
- **AAKP Veterans Health Initiative**
- **Engagement and Skills Training** (web-based/in-person)
  - Print Media
  - Social / Online Media
  - Radio & Broadcast
  - Patient Advisory Boards
- **Speakers Bureau: Patient/Living Donor/Caregiver** (conferences, industry meetings, town hall meetings, interviews, media)
- **Membership Services**
- **Flash surveys/questionnaires**
- **The Decade of the Kidney™** (AAKP initiated and led)
- AAKP Global™
- **Social Media**
  - Facebook @kidneypatient
  - LinkedIn American Association of Kidney Patients
  - X/Twitter @kidneypatients
  - YouTube @americanassociationofkidne3513e
- **Peer Mentor Program**

Advocacy

- Public Policy Summit (virtual/in-person)
- Public Policy Roundtables (virtual/in-person)
- AAKP National/State Patient Advocacy Day/ Capitol Hill Day Visits (virtual/in-person)
- AAKP Action Center
- KidneyVoter™ (register to vote campaign)
- Patient Voice Patient Choice™
- Government Déterminants of Health (GDoH)
- Advocacy and Skills Training (web-based/in-person)
  - Policy Analysis
  - Effective Advocacy
  - Voter Engagement Mobilization
  - Comment letter writing
- How to Become Your Own Public Policy Advocate (brochure)
- Action Alerts
- Targeted Press Releases
- Legacy Awards Program
- Patient Engagement & Advocacy Awards Program
- Public Service & Congressional Awards Program

Center for Patient Research & Education

Research	Education

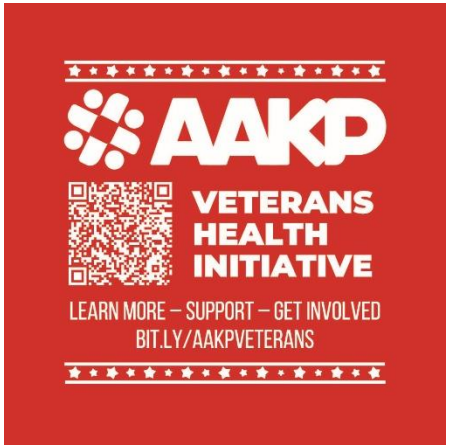
• **Global Summit on Kidney Innovation** (virtual/in-person)
• **Research and Skills Training Sessions**
  ○ Research
  ○ Technical Writing
• **Clinical Trial Awareness Campaigns**
• **Market Research Recruitment**
• **Geographic targeting of patients for specific engagement efforts**
• **Demographic targeting of patients for specific engagement efforts**
• **AAKP Constituent Database** (continual data collection)
• **Patient Advisory Panels/Councils**
• **Patient Roundtables**
• **Focus Groups** (web-based/in-person)
• **Direct patient interviews** (one-on-one)
• **Patient surveys** (web-based/telephone)
• **Fabry Disease Diagnostic Testing Project**
• **AAKP Intergalactic™**
	• AAKP Website (www.aakp.org)
	• AAKP Shared Decision Making Guide (print/online)
	• COVID-19 Education/Resource Center
	• National Patient Meeting
	• Medal of Excellence Award Program
	• Pocket Guide series (print/online programs)
	• Nutrition Program/AAKP Delicious! (print/online/App programs)
	• Kidney Beginnings series (print/online/interactive programs)
	• Patient Plan series (print/online/interactive programs)
	• aakpRENALIFE (national magazine)
	• Kidney Beginnings (e-newsletter)
	• Kidney Transplant Today (e-newsletter)
	• aakpRENALFLASH (e-newsletter)
	• At Home with AAKP (e-newsletter)
	• AAKP Pediatric Kidney Kids (e-newsletter)
	• HealthLine (webinar program)
	• HealthLine Innovator (webinar program)
	• Cystinosis Patient Scholarship Program
	• Patient Safety Award Program
	• National High Potassium Awareness Day – “Are You O-K+” campaign (hyperkalemia)
	• National Itch Day – “Stop the Itch” campaign (CKD-aP)

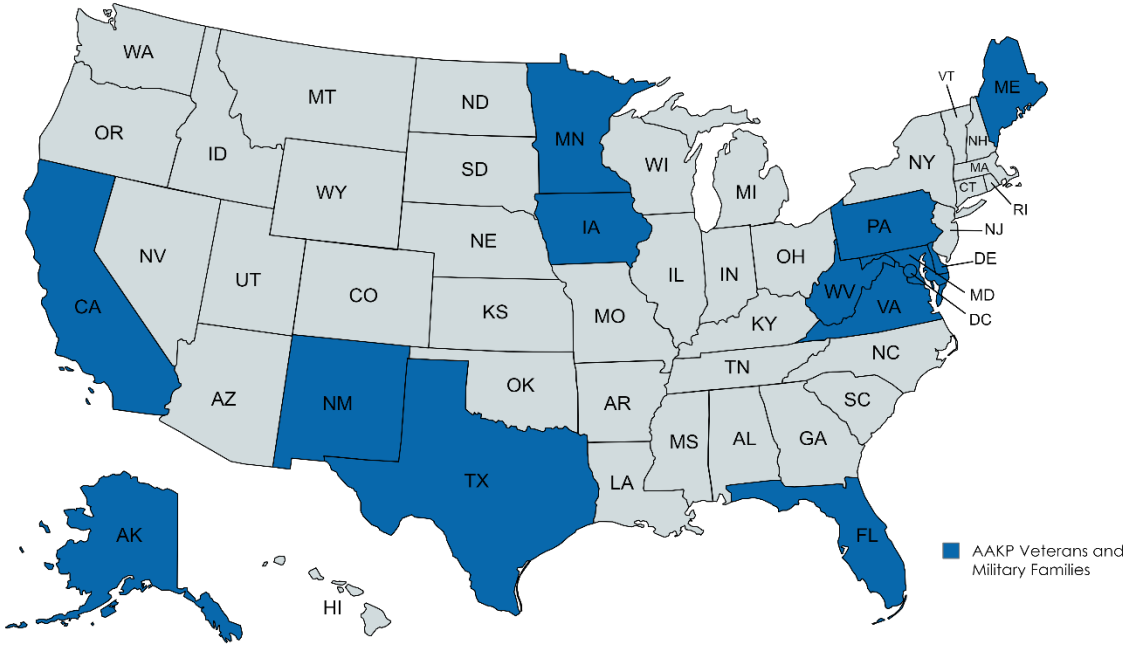
AAKP Veterans Health Initiative

https://bit.ly/AAKPVHI

Objectives:

- Advance research, innovation and policies aimed at safeguarding the highest standards in kidney care and treatment for veterans managing kidney disease.
- Allow fellow veterans to have their voices heard, retain access to the care they have earned and are legally entitled to at the VA and elsewhere.
- Gain the benefit of new research and innovations in the realms of biologics, diagnostics, and devices.



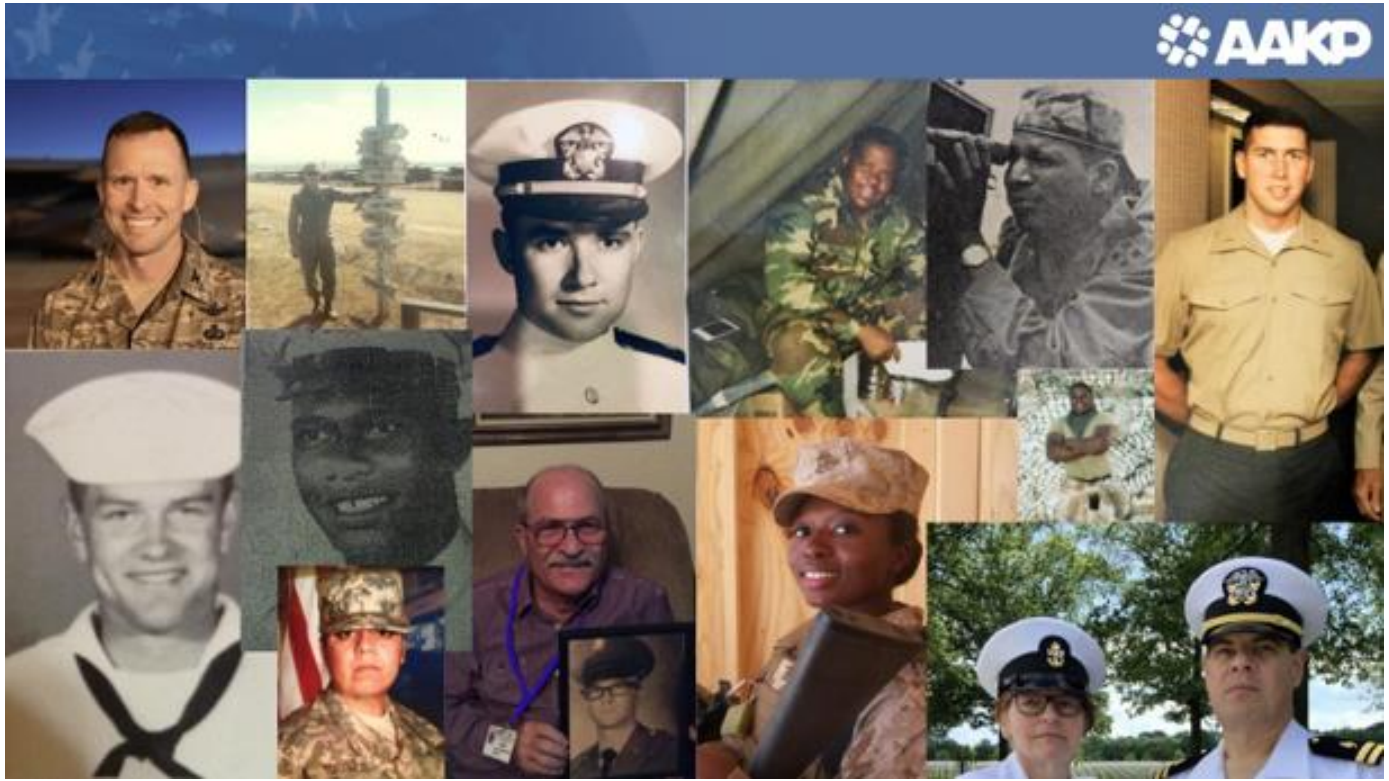


AAKP Veterans and Military Families in:

- Alaska
- California
- Delaware
- Florida
- Iowa
- Maine
- Maryland
- Minnesota
- New Mexico
- Pennsylvania
- Texas
- Virginia
- Washington, DC
- West Virginia

Through AAKP's Center for Patient Research and Education, AAKP's Veterans Health Initiative remains involved in a number of VA research projects.

Project Title	Lead Institution(s)	Principal Investigator	Project Term	Website
Beta Blocker Dialyzability on Cardiovascular Outcomes (BRAVO)	Minneapolis VA Medical Center Manhattan Campus, VA NY Harbor Healthcare System	Areef Ishani, MD James S. Kaufman, MD	January 2024 - December 2027	**Learn more**
Medicaid expansion and quality, utilization and coordination of health care for Veterans with chronic kidney disease	VA Central Office	David Atkins, MD Laura A. Peterson	April 2021 - September 2025	**Learn more**
Diuretic Comparison Project (DCP)	Minneapolis VA Medical Center Memphis VA Medical Center	Areef Ishani, MD William Cushman, MD	June 2016 - October 2022	**Learn more**


AAKP

@kidneypatient

@kidneypatients

@kidneypatients

bit.ly/AAKPYouTube

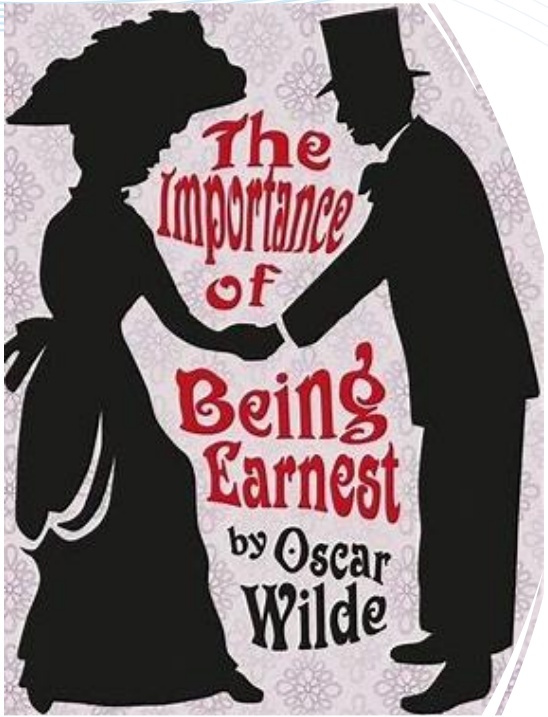
American Association
of Kidney Patients

American Association of Kidney Patients

14440 Bruce B. Downs Blvd.
Tampa, FL 33613
www.aakp.org

Edward V. Hickey, III
ehickey@aakp.org

THE IMPORTANCE OF BEING EARNEST: PROVIDER ENGAGEMENT IN PRAGMATIC ESKD RESEARCH



James Kaufman, MD (on behalf of Susan T Crowley, MD, MBA, FASN)
Principal Investigator, CSP 2026 DiaP & BRAVO
Staff Physician, Division of Nephrology
VA New York Harbor Healthcare System
Professor of Medicine
NYU Grossman School of Medicine

VA | U.S. Department of Veterans Affairs

Disclosures

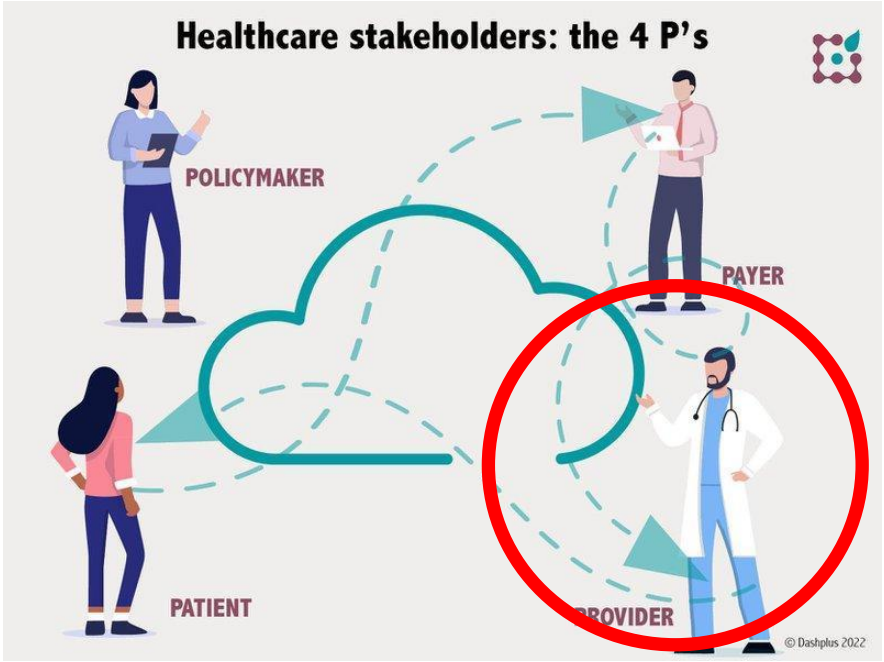
- Consultant fees – NIDDK, Otsuka Pharmaceutical, Cymabay Therapeutics, Inc.
- Associate Editor, American Journal of Kidney Disease

Provider Stakeholder Engagement -Overview

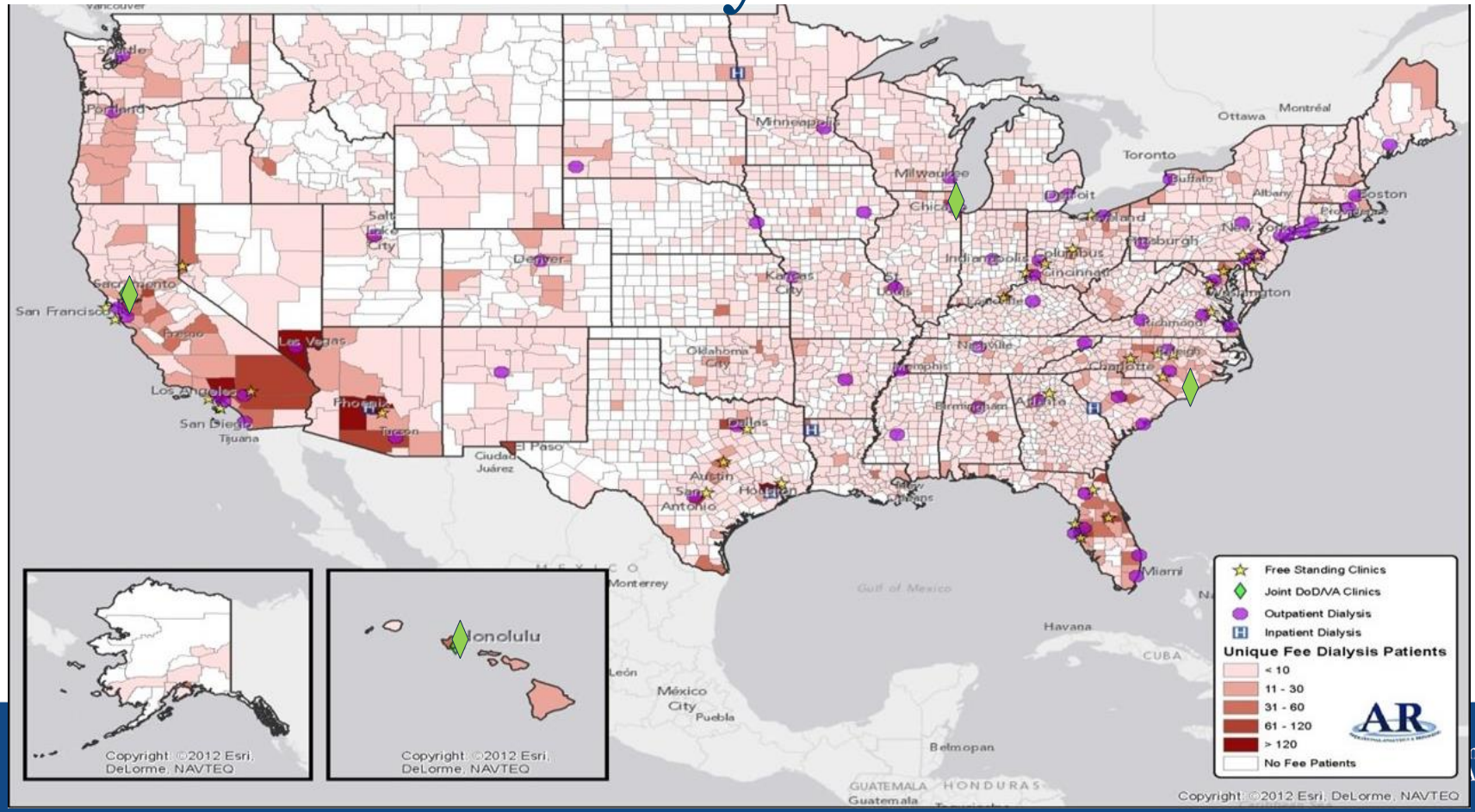
- Published literature indicates a critical need for “stakeholder” engagement in clinical research, especially pragmatic research.
- First, who are the “stakeholders” in the VA BRAVO pragmatic trial?
- Second, why is *clinical provider* stakeholder engagement critical?
  - Lessons learned from previous/ongoing pragmatic studies in ESKD population
- Strategy for *clinical provider* engagement in VA BRAVO

Who are the Stakeholders in BRAVO Study?

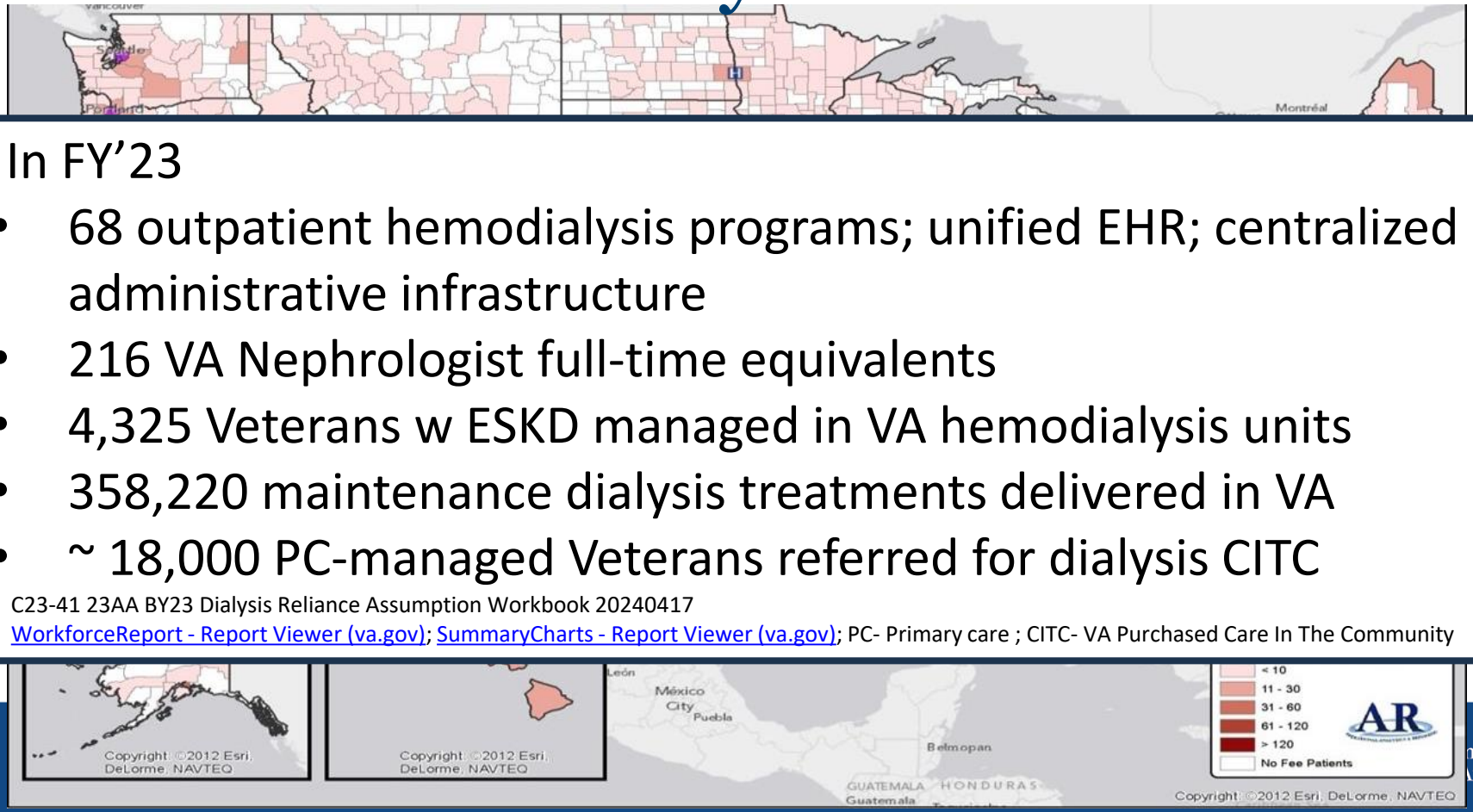
- Patients
- Clinical “Providers”
  - Medical Facilities
  - Clinical Staff
    - Dialysis Directors& Providers
    - Dialysis Nursing & Technicians
    - Allied Staff – PharmD, RD, SW
    - Primary Care Providers
- Policy-makers
  - Executive Leadership
- Payers
  - Congress



VHA Dialysis Units



VHA Dialysis Units

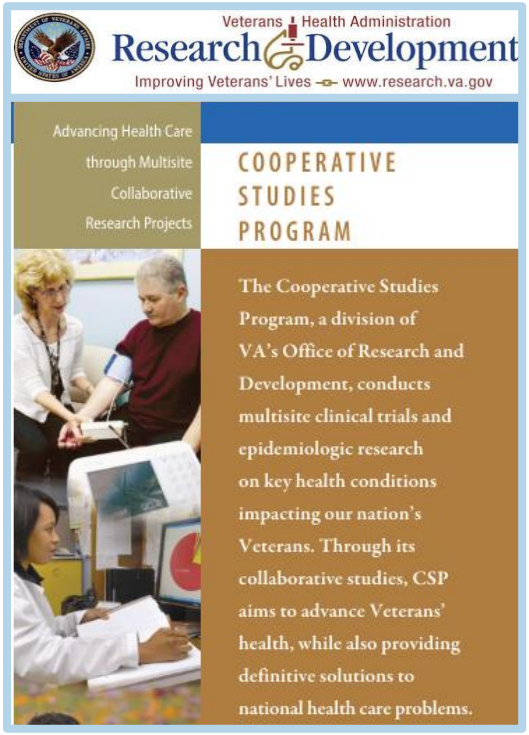


- In FY'23
  - 68 outpatient hemodialysis programs; unified EHR; centralized administrative infrastructure
  - 216 VA Nephrologist full-time equivalents
  - 4,325 Veterans w ESKD managed in VA hemodialysis units
  - 358,220 maintenance dialysis treatments delivered in VA
  - ~ 18,000 PC-managed Veterans referred for dialysis CITC

C23-41 23AA BY23 Dialysis Reliance Assumption Workbook 20240417

WorkforceReport - Report Viewer (va.gov); SummaryCharts - Report Viewer (va.gov); PC- Primary care ; CITC- VA Purchased Care In The Community

VA Research in Veteran ESKD Population



- Select VA Cooperative Study Trials in ESKD
  - Subcutaneous compared with intravenous epoetin in patients receiving hemodialysis. DVA CSP Group on Erythropoietin in HD Patients. *NEJM*.**1998**. doi: 10.1056/NEJM199808273390902
  - Randomized controlled trial of clopidogrel + aspirin to prevent hemodialysis access graft thrombosis. *JASN*.**2003**;doi:10.1097/01.asn.0000081661.10246.33
  - Effect of homocysteine lowering on mortality and vascular disease in advanced chronic kidney disease and ES[K]D: a randomized controlled trial. *JAMA*.**2007**;. doi:10.1001/jama.298.10.1163.

Why clinical provider stakeholder engagement?
Previous *Pragmatic Study in ESKD Population*

TiME: A Fully Embedded Pragmatic Trial of Hemodialysis Session Duration

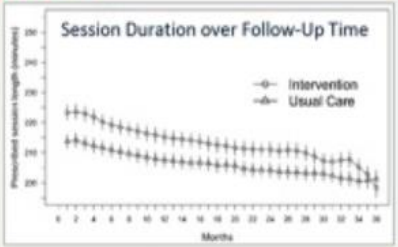
METHODS

Pragmatic Features
- Broad eligibility criteria
- Intervention implemented by clinicians
- All data acquired through routine clinical care
- No on-the-ground research personnel

- 266 dialysis units: FMC-NA and DaVita
- Single IRB of Record
- Opt-out consent

RESULTS

- >7000 participants enrolled ahead of schedule
- Opt-out rate was <1%
- Participant characteristics closely matched the US dialysis population
- Uptake of the intervention was not sufficient to determine impact of longer sessions on outcomes



Primary Analysis Population	Intervention	Usual Care
Deaths per 100 patient-yr	19.2 (17.4, 21.0)	19.7 (18.1, 21.4)
HR (95% CI); p Value	0.97 (0.84, 1.12); 0.69	
Hospitalizations per 100 pt-yr	204.5 (186.9, 223.7)	214.1 (202.5, 226.3)
Rate ratio (95% CI); p Value	0.96 (0.86, 1.06); 0.40	

CONCLUSION

A highly pragmatic design allowed efficient enrollment, data acquisition, and monitoring but intervention uptake was insufficient to determine whether longer hemodialysis sessions improve outcomes. Effective strategies for engaging clinical personnel and patients are required to evaluate interventions fully incorporated into care delivery.

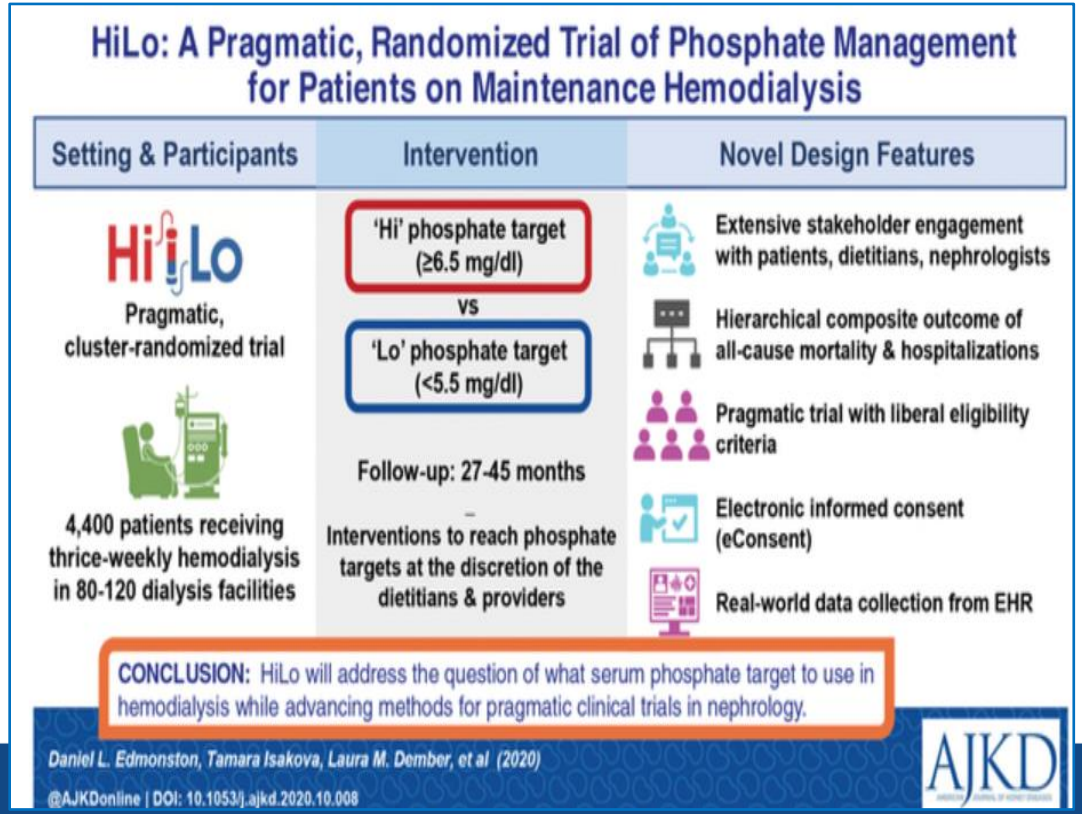
Clin Provider Stakeholders

- Dialysis Organization
  - Assent to randomized paradigm of > 4.25hr vs usual care
- Nephrologists
  - Assent
  - Manage all other aspects of dialysis

JASN doi: 10.1681/ASN.2019090945

Why clinical provider stakeholder engagement ?

Ongoing *Pragmatic Study in ESKD Population*



Clinical Provider Stakeholders

- Dialysis Organizations
  - Assent, staff education of aims of HiLo
  - Submission of monthly data transfers (labs,death, hosp) via Hi Lo IT portal
- Nephrologists
  - Assent; staff education re aim of HiLo
  - Prescribe Phos Binder
  - Manage all other aspects of dialysis
- Dieticians
  - Design of Hi-Lo /Steering Cmte rep
  - Dietary &Phos binder titrate reccs
  - Review facility/pt achieved Phos report
  - Patient Counselling re achieved Phos
  - List mgmt of pts approach/consented
  - Facilitate e-consent via preloaded tablet
  - NOT engaged in research from regulatory standpoint

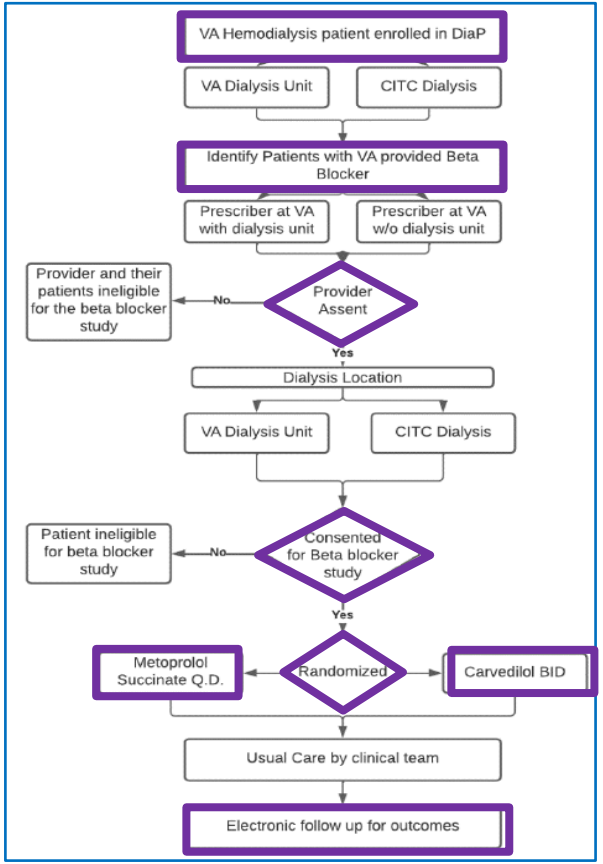
What have we learned from pragmatic studies in ESKD about the value of clinical provider stakeholder engagement ?

- Lessons echoed pragmatic research in non-renal fields that the benefits of stakeholder engagement include:
  - Gathering meaningful ***input*** on study design and implementation,
  - Gleaning insights into ***balancing*** the need for flexibility among clinical sites
  - Facilitating implementation of interventions with ***fidelity***
  - Encouraging discussion about ***program sustainability*** and dissemination
  - ***Priming*** health system for successful change in clinical practice enterprise-wide

- Critical to successful clinician engagement – ***clinician centric approach***
  - Dynamic integration of intervention ***within*** existing workflows
  - Facilitated educational support for clinician ***learning***
  - ***Minimize burden*** of clinician by leveraging technology (data transfer, e-consent,)
  - ***Focus*** on important CKD outcomes

Strategy for clinical provider stakeholder engagement in VA BRAVO

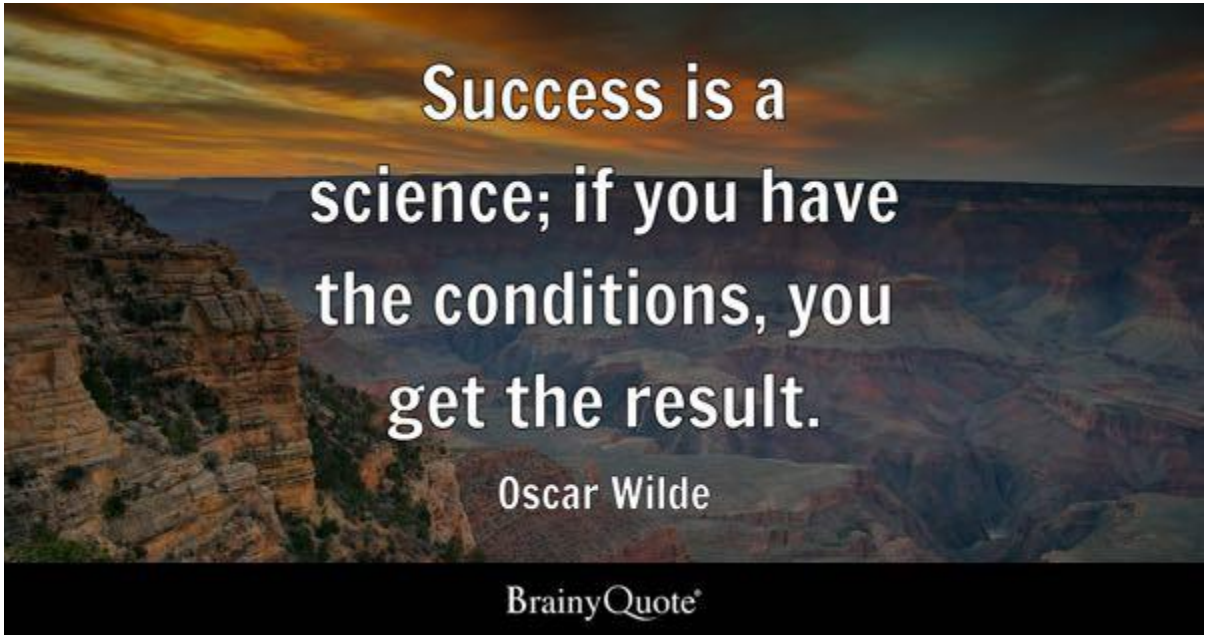
- **Provider education for Upfront Buy-in**
  - Established communication channels for VA Kidney Medicine & PC
    - BRAVO rationale/relevance to Veteran health
    - Pragmatic paradigm & VA Dialysis Platform
- **Vertical integration & communication**
  - Implementation interviews with providers to maintain engagement
- **CSPCC centralized functions**
  - + VA cIRB approval & LSRO notification



CSPCC= Cooperative Studies Program Coordinating Center
LSRO-Local Site Research Office

Summary

- Pragmatic clinical research aims to efficiently define the real-world impact of relevant clinical interventions.
- Real-world impact of health care is dictated by clinical providers, thus they are essential stakeholders to consider for the optimal design and execution of pragmatic research, and ultimately for priming the health system for widespread adoption of effective interventions
- Lessons learned from previous ESKD focused pragmatic studies about clinical provider stakeholder engagement have been applied to the development of the VA BRAVO/DiaP Study.
- Building on these lessons, the BRAVO/DiaP study will be better poised to identify which options of usual care for people with ESKD are best and distinguish VA as a national *kidney* learning healthcare system.


Success is a science; if you have the conditions, you get the result.
Oscar Wilde
BrainyQuote

BRAVO - KEYS TO SUCCESS AND DISSEMINATION PLAN

James Kaufman, MD
Principal Investigator, CSP 2026 DiaP & BRAVO
Staff Physician, Division of Nephrology
VA New York Harbor Healthcare System
Professor of Medicine
NYU Grossman School of Medicine

VA | U.S. Department of Veterans Affairs

Objectives

- Barriers to Success
- Keys to Success
- Overcoming Barriers to Success
- Barriers to Implementation
- Overcoming Barriers to Implementation
- Implications for Other Studies

Barriers to Success

Why Clinical Trials Fail

- Failing to demonstrate efficacy or safety
- Participant recruitment
- Participant burden
- Financial impact

Fogel DB. Contemp Clin Trials Commun 2018; 11”156-164


LOWERING BARRIERS

How Pragmatic Comparative-Effectiveness Trials Minimize These Burdens

Cause	Comparative Effectiveness Trials
Failing to demonstrate efficacy or safety	Any outcome clinically meaningful
Financial impact	Pragmatic trials are low-cost
Eligibility criteria	Broad eligibility criteria
Participant recruitment	Central recruitment / Waiver of consent
Participant burden	No study visits / Outcomes from EHR
Ineffective site selection	Broad range of sites

Strategies to Improve Enrollment

- Education
- Improve information on potential trials
- Improve trial infrastructure
- Incentivize trial participation
- Make randomization easy

Fidelity to Intervention

Using “Real Word” Data

Accurate Outcome Ascertainment

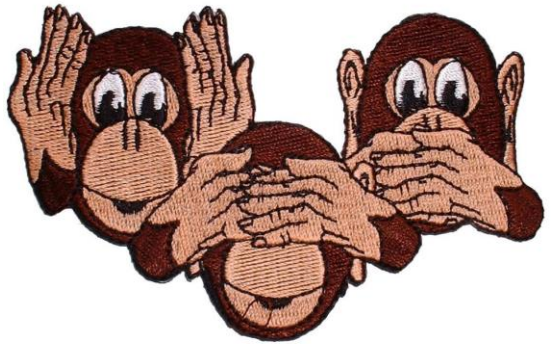
- Death
- Acute decompensated heart failure
- Acute stroke
- Acute myocardial infarction

Huang H et al. Am J Cardiol 2017; Raju S et al. Contemp Clin Trials 2023; 130:107214; Davidson J et al. Clin Epidemiol 2020; 12:1095

DISSEMINATION AND IMPLEMENTATION PLAN

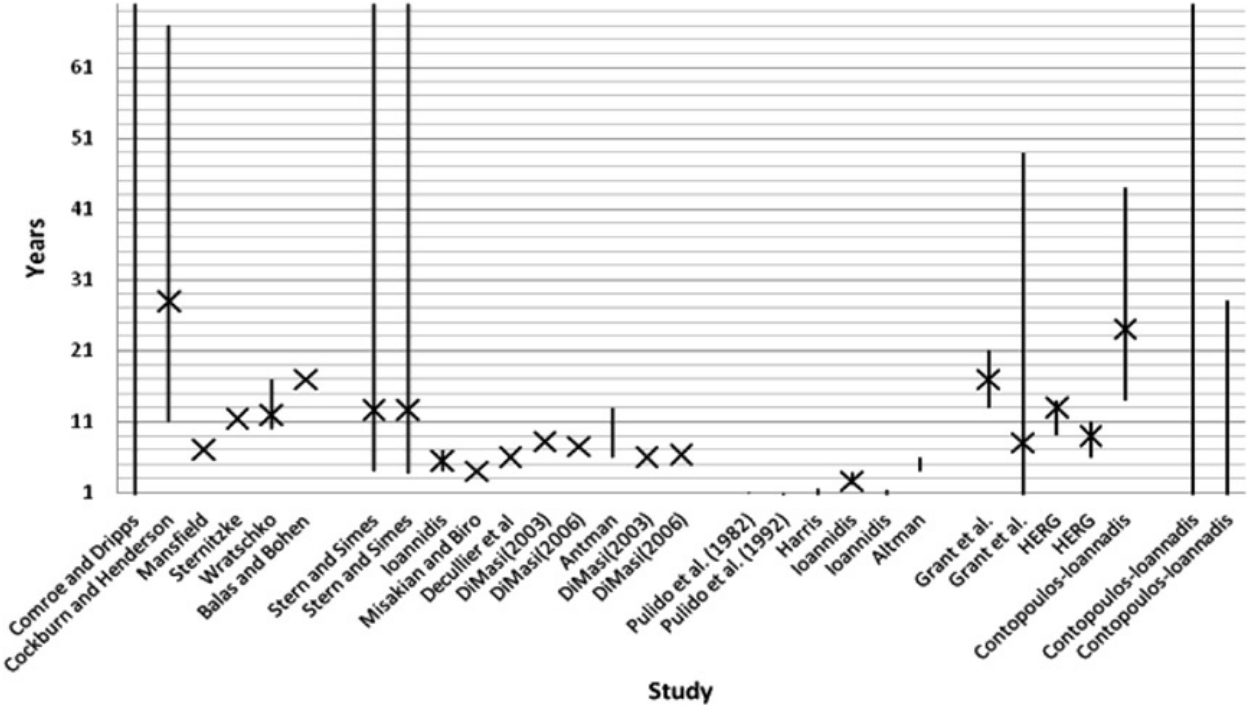
Evidence to Practice Gap

NEJM



Morris SJ. Wooding S, Grant J. J R Soc Med, 2011; 104:510-520.

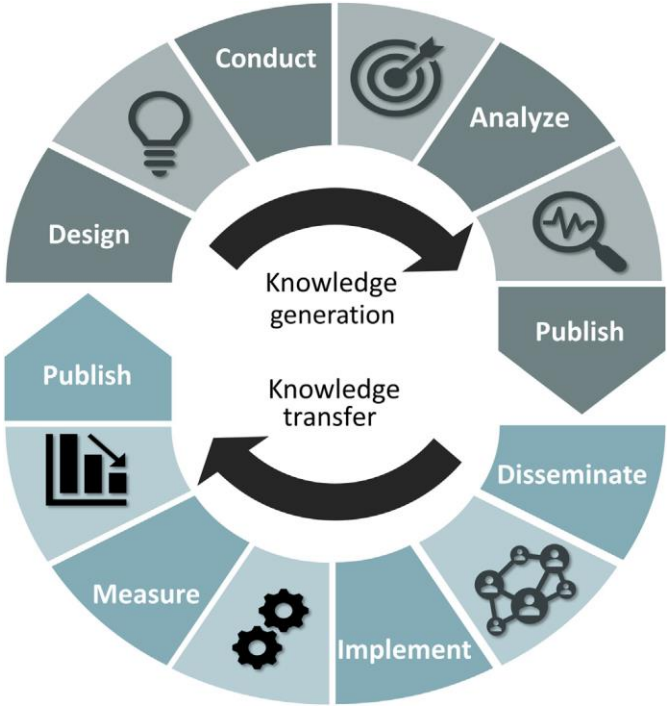
Time Lag in Health Research



Dissemination and Implementation Plan

- Dissemination - targeted distribution of information and intervention materials to a specific audience
- Implementation - the use of strategies to adopt and integrate evidence-based health interventions and change practice patterns

Publication Is Not the End



Reidlinger DM et al. Kidney Intern 2022; 102:1222-1227

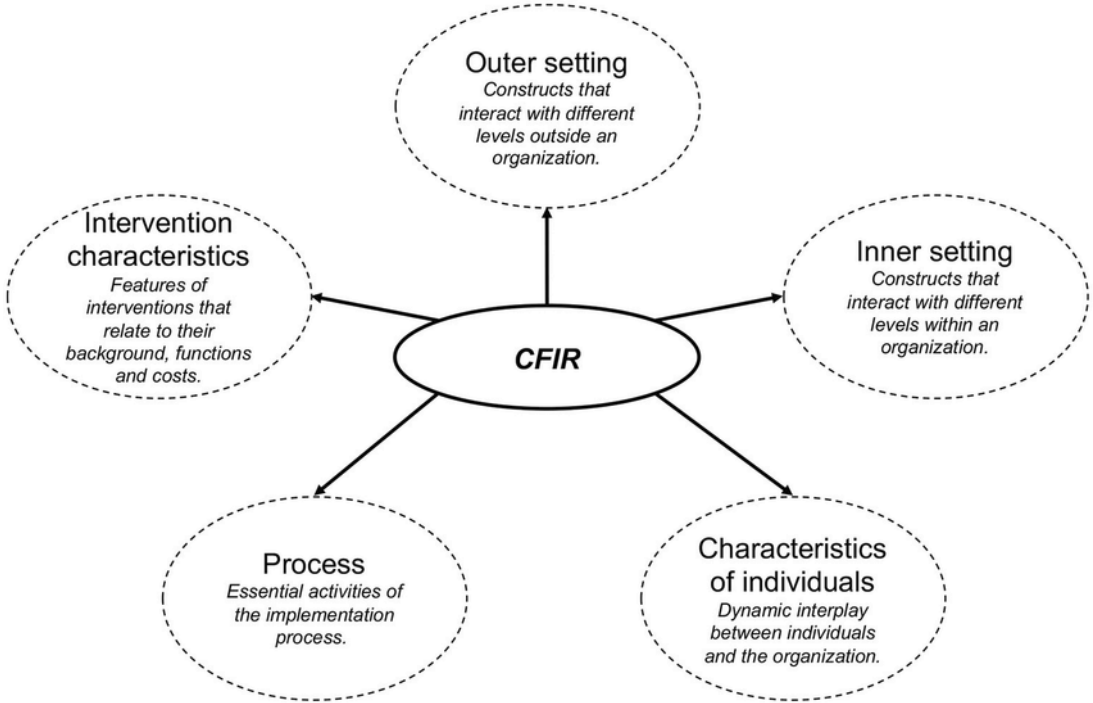
Actions to Enhance Implementation of Trial Results



Design	Conduct	Report
Partner with consumers	ITT analysis	Results published
End-user engagement	Intervention easy to implement	Data sharing policy
Pragmatic protocol	Process evaluation conducted with clinicians and participants	Declaration of competing interests
Outcomes collected through EHR	Outcomes meaningful to stakeholders	Lay language summaries relevant to stakeholders
Comparator based on current clinical practice	Protocol published	Presentation at major meetings and through social media

Implementation Research Questions

- What are provider and system-level barriers and facilitators to adoption, implementation, and sustainment of trial-based evidence
- What changes are made by practices to implement the trial, and how effective are these changes in improving adoption, implementation and sustainment of the changes



Damschroder LJ et al. Implementation Sci 2009; 4:50

Advantages of VA Healthcare System

- Common EHR with central data storage
- Common formulary
- Supportive leadership
- Experience in large pragmatic trials
- Patient population willing to participate in research
- Develops disease-specific clinical practice guidelines

BRAVO Dissemination and Implementation Plan

- Guidelines and quality indicators
- Training in clinical processes and evidence-base quality improvement
- Marketing
- Centralized infrastructure for long-term support of dissemination and implementation

Guidelines and Quality Indicators

- Update CPG for VA and nephrology organizations
- Adopt performance indicators to incentivize best practices within the VA and with contractors
- Assess fidelity over time
- BRAVO Executive Committee will gain experience in dissemination and implementation and will be able to advise others regarding updates to indicators, measurements, fidelity, and sustainability of change

Training in Clinical Processes and Evidence-Based Quality Improvement

- Develop training materials
- Create an online dose calculator
- Develop tools for assessing site needs prior to implementing the BRAVO model
- Identify and develop needed implementation tools and strategies including with opinion leaders and providers

Marketing

- Identify relevant stakeholders and develop a marketing plan to promote the spread of BRAVO intervention to new VA networks and facilities
- Disseminate scientific findings related to the implementation
- Recruit four new VA networks to begin implementing the proposed dissemination and implementation program by Study Year 2 and at least 10 more by Study Year 3
- Collaborate with academic detailing and the dialysis community of practice

Centralized Infrastructure & Sustainability

- Develop centralized infrastructure for long-term support of dissemination and implementation for future Dialysis Platform projects

Evaluation of Dissemination and Implementation Activities

- Primary outcome is the quantitative proportion of dialysis patients on beta blockers receiving the appropriate evidence-based treatments
- We will calculate these proportions monthly at levels of provider, facility, VISN, and national as well as by provider and patient characteristics
- Qualitative analysis from final round of qualitative interviews to identify themes regarding the implementation process, including barriers and facilitators to making anticipated changes and strategies used by clinics to make changes

QUESTIONS