Diuretic Comparison Project Case Example: Learning from an Integrated Health System

Embedding trials into health care delivery is possible. CTTI spoke with individuals from five different trials in which certain elements of the trial were embedded into clinical practice. We provide an example of one trial, the Diuretic Comparison Project, below.

TRIAL OVERVIEW

▶ Randomized, open-label trial

▶ Number of sites: 72 (all sites within U.S. Veteran's Affairs)

▶ Number of patients enrolled: 13,523

▶ Ages eligible for study: Older Adult (65 years and older)

▶ Interventions: Drugs (Hydrochlorothiazide vs. Chlorthalidone) for hypertension

▶ Primary outcome/endpoint: time to major cardiovascular event (event composite consisting of: stroke, myocardial infarction, non-cancer death, urgent revascularization, and hospitalization for acute congestive heart failure; modified MACE)

EMBEDDED TRIAL ELEMENTS

▶ *Patient Identification & Eligibility*: Identified, enrolled and followed patients using the electronic health record (EHR) and national VA and non-VA databases (e.g. Medicare, NDI)

▶ *Data Acquisition*: Aligned outcomes and endpoints to data captured within routine care (appreciating the level of structured data existing and needed)

▶ The trial also aligned research requests with clinical workflow to have minimal burden for providers (i.e. titrated the number of patients the providers could see to minimize 'alert fatigue' among providers; asked provider for 3 simple research related clicks in EHR: willingness to consent, assent to be a participant, and the drug order)

▶ *Intervention*: All patient care, including the study drug, are managed by the primary care provider; Intervention is prescribed through the EHR (entered by research nurse and co-signed by the patient's provider) and mailed directly to patient or had order ready at a local pharmacy

WORDS OF WISDOM

▶ Engage stakeholders early in study design including hospital executives and chiefs, health care providers, EHR programmers, and patients.

▶ Understand the clinical work flow and reduce burden on the providers.

▶ Build in lag time for "delayed" data sources in the study design.

▶ Assess risk of missing data through completeness and accuracy checks.

▶ Align participation incentives and communicate the value of a learning health care system to enable necessary buy-in.

▶ Find a champion at the local site.

	CHALLENGES	SOLUTIONS
Technology Infrastructure	Difficulty randomizing within the EHR (i.e. difficult to do a complicated randomization)	Opted for blocked randomization that occurs outside of the EHR and coordinated by research nurses at central coordinating site
Data	Delay in availability of certain data sources (e.g. Medicare) which could risk data completeness	Used structured data elements in the design of the study Assessed missing data through completeness and accuracy checks
Culture	Some sites and providers were uncomfortable with external people putting orders into the system, despite being credentialed clinicians within the VA	Engaged providers early on and gave clinical autonomy by seeking their consent to screen their patients, and assent agreement to participate on an individual level Clearly communicated expectations for each side
Process	It takes time and buy-in to get a workflow system in order, initiate a site, and flag data appropriately	Started small (locally only) and naturalistically, then rolled out over time Stayed flexible and allowed for constant iterations after study began