Statistical Analysis Plan

Electronic Alert-Based Computerized Decision Support to Improve Testing For Primary Aldosteronism in Patients with Hypertension (ALERT-PA)

NCT05925569

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ALERT-PA Statistical Analysis Plan

1) Study Design: Cluster-randomized controlled trial

Intervention = Computer decision support alert
Control = Usual care (silent alert/not shown to clinician)

Analysis level = Individual patient
Randomization level = Clinician, randomized by NPI # (even vs odd, approx. 1:1) to Active vs Silent Alert

2) Outcomes:
   i. Primary Outcome = Odds/Rate of ordering Aldo/Renin labs
   ii. Secondary Outcomes
      a. Rates of ordering e-consult
      b. Rates of referral to relevant specialist (endocrine, renal, cardiology)
      c. Rates of initiation of MRA
      d. Rates of new PA-related diagnostic code
   iii. Exploratory Outcomes
      a. Change in average SBP (3 last SBP prior to intervention and 3 first after intervention)
      b. Rates of labs completed
      c. Rates of possible and likely PA based on newly ordered labs (definitions per PA Screen, plus rates of low renin and low-renin among ACE/ARB)
      d. Rates of prior completed PA testing, number of instances of prior testing per patient
      e. Among prior testing, rates of possible and likely PA (with alternative definitions as above in “c”)
      f. Dose-response re # of alert firings & primary outcome
      g. Subgroup analyses – rates of primary outcomes by:
         i. Clinician specialty (Gen med, Cardiology, Endo, Nephro)
         ii. Clinician type (NP, PA, MD)
         iii. Clinical site (Main BWH, satellite, Harbor med)
         iv. Those with vs without prior testing
         v. By race/ethnicity; sex; CKD y/n; age <50, 50-80, >80 (or other?)

3) Covariates:
   i. Patient Level:
      a. Demographic Characteristics: Age, sex, gender identity, BMI, Race, Ethnicity, Level of Education, Primary Language, Insurance type
      b. Medical history – by dx code: CAD, CHF, Stroke, CKD (one or two eGFR<=60 measured >90d apart), PAD, DM (by code or two A1c>=6.5% at least 9mo apart), HLD
      c. Recognized secondary hypertension – by dx code
      d. BP meds – total number and number of each class
      e. Ever treated with an MRA
      f. Rx for KCl supplement – binary use, total daily dose

g. Labs: Lowest Potassium value (outpatient), Last potassium value, last eGFR

ii. Clinician Level:
   a. NPI number/ID
   b. Specialty
   c. Practice Type (BWH/AMC, Satellite/community, Harbor Med)
   d. MD/NP/PA
   e. Number of patients enrolled
   f. Number of alerts per patient

Power Calculation (from Detailed Protocol)
Based on prior randomized controlled trials of alert-based CDS tools, we conservatively estimate that the BPA notification will increase screening for PA by 2-fold in patients meeting guideline-based criteria. Assuming a baseline rate of screening of approximately 4%, we estimate that we will need 800 patients in each group (total sample of 1600) to detect a 2-fold increase in the rate of screening with 80% power at a two-sided alpha of 0.05, assuming approximately 4 patients per cluster and an intraclass correlation coefficient of 0.1.

However, based on early pilot testing of the study CDS alert running in Epic shadow mode, we discovered that the initially proposed sample size of 1600 would accrue too quickly, with approximately 200 potentially eligible patients per day resulting in only an 8-day study enrollment period. Given there is no additional risk to patients or clinicians by expanding the sample size, we will instead continue enrollment for a fixed 12-week duration to maximize study validity, with the final sample size dependent on the number of patients who ultimately meet eligibility criteria and present for qualifying clinical appointments with eligible providers over the 12-week enrollment period.

Statistical Analysis

Descriptive Statistics:
Provider and patient baseline characteristics
Test balance between intervention and control groups using generalized estimating equations

Primary analysis:
Null hypothesis: The computer alert did not impact the odds of ordering PA screening labs.
Alternative Hypothesis: The computer decision alert increased the odds of ordering these labs.
Approach:
General linear mixed model – Labs ordered(y/n) = Intervention Arm (active vs silent alert) with random effects for clinician, clinician specialty
Unadjusted model and then adjusted model including patient and provider characteristics that are imbalanced between the groups on baseline comparison as fixed effects.

Secondary & Exploratory Analyses: Same structure as above. No plan for adjustment for multiple testing or dividing alpha, given secondary/exploratory.

Exploratory Analysis – Impact of Repeat Alerts:
Clinicians randomized to the active alert would receive repeat alerts every time the same patient returned to the office within the 6mo intervention. Once they ordered labs via alert, it stopped.
Null Hypothesis: There was no impact of repeat alerts on the rates of ordering PA labs.

Alternative Hypothesis: There was a dose-response relationship where the more alerts fired per patient, the more likely they were to have the labs ordered.
Approach: General linear mixed model as above with # of prompts per clinician included as a covariate

Missing Data:
Complete case analysis
Multiple imputation
Rate of missingness is low overall: <1% for demographics, <2% for BPs, 2-5% for labs, 0% for diagnoses, meds, and outcome measures.