**Study Title:** Patient Portal Reminder/Recall for Influenza Vaccination in a Health System- RCT 3

**Initial IRB Approval:** 12/20/2017

**RCT 3 IRB Approval:** 8/14/2020

**Clinical Trials Registration:** NCT04533685

## Statistical Analysis

*Primary Analysis*

We hypothesize that patients receiving pre-commitment prompts will have higher vaccination rates than control arm patients; patients sent pre-appointment reminders will have higher vaccination rates than control arm patients; and patients linked to direct scheduling will have higher vaccination rates than control arm patients. Primary outcomes (patient receipt of flu vaccine) are binary; our main explanatory variable will be an indicator for the receipt of any portal-based R/R or prompt.

The analysis will be based on a 2x2x2 nested factorial design, nested in a parallel 2-arm trial RCT, comparing the effectiveness of combining portal R/R with patient direct appointment scheduling vs. portal R/R alone vs. control (no intervention) on influenza vaccination rates. Both treatment groups will be additionally randomized into 4 groups to receive 1) a R/R message only (with or without direct appointment scheduling link), 2) the R/R message and a pre-commitment prompt, 3) the R/R message and pre-appointment reminder or 4) the R/R message, a pre-commitment prompt, and a pre-appointment flu vaccine reminder.

We will employ intent-to-treat analyses using mixed effects log-binomial regression models with practice random effects, an approach recommended for RCTs in which the goal is to estimate the causal effects of interventions on individuals, adjusted for clustering of patients by practice. The primary model terms will be general reminder arm (general reminder v. no general reminder), and interactions between general reminder arm and (1) pre-commitment arm (pre-commitment question v. no pre-commitment question), (2) pre-appointment reminder arm (pre-appointment reminder v. no pre-appointment reminder) and (3) direct scheduling arm (general reminder links v. does not link to direct scheduling).). Models will adjust for the following patient characteristics: age, gender, race/ethnicity, primary language, primary insurer, and prior receipt of influenza vaccines in the last two years. Evaluation of study hypotheses will be performed using model contrasts, and treatment effects will be reported in terms of risk ratios and 95% CIs. In the event of computational issues, we will replace the log-binomial specification with a log-Poisson specification, and use model-robust standard errors for inference on treatment effect risk ratios.

*Secondary Analysis*

Secondary analyses will include evaluation of process measures (e.g., missed opportunities); evaluation of effect modification by patient characteristics; comparison of receiving pre-commitment intervention and pre-appointment reminder intervention with not receiving those interventions, however still receiving reminder letters; and evaluation of vaccination receipt including self-reported vaccinations. Process measures will be analyzed similarly to the primary outcome, but using different distributions and link functions as appropriate (e.g., negative binomial distributions for number of missed opportunities). Effect heterogeneity will be evaluated by introducing interaction terms into the primary model specification. All secondary

analyses will use a significance level of 0.05. All analyses will be performed using SAS v. 9.4 (SAS Institute Inc., Cary, NC).

Process measures: We assessed the percentage of patients who opened the portal reminder letter, as well as the source of influenza vaccination data (health system within UCLA practices, external source via data transfer, patient/proxy update through normal portal processes, or patient/proxy update in response to portal reminders.