Alerts with Risk Information to Increase Influenza Vaccinations

Statistical Analysis Plan

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Scientific Background and Objectives

The CDC (Centers for Disease Control) recommends a flu vaccination to everyone aged 6+ months, with rare exception; almost anyone can benefit from the vaccine, which can reduce illnesses, missed work, hospitalizations, and death. One barrier to vaccination is a lack of "cues to action," and, in particular, the lack of direct recommendation from medical personnel; this barrier is arguably most effectively overcome by a simple nudge of clinicians, compared with barriers such as negative attitudes toward vaccination, low perceived utility of vaccination, and less experience with having received the vaccine.

Geisinger partnered with Medial EarlySign (Medial) to develop a machine learning (ML) algorithm to help identify people at risk for serious flu-associated complications based on existing electronic health record data. Eligible at-risk patients were randomized to an active control group (clinician is shown a standard flu alert) or one of two experimental groups (clinician is shown an alert indicating patient's high risk, with or without describing the patient's factors contributing to that risk).

Methods

Patients in the top 20% of risk for flu and complications, according to Medial's algorithm, were pre-randomized into the following arms:

1. Standard Alert: For flu-shot best-practice alert (BPA)-triggering appointments, the standard flu-shot BPA fires.
2. High-risk Alert: For BPA-triggering appointments, a modified BPA fires. This BPA includes salient features (e.g. larger alert headers, bold face, red font), and alerts the clinician that the patient is at high risk for flu and its complications.
3. High-risk Alert with Risk Factors: For BPA-triggering appointments, a modified BPA fires. This BPA includes salient features (e.g. larger alert headers, bold face, red font), and alerts the clinician that the patient is at high risk for flu and its complications. This BPA also presents the top factors contributing to the patient's high risk.

Patients are subsequently enrolled in the study if they attend at least one appointment where their assigned flu-shot BPA fired.

Clinicians are enrolled if they see a flu-shot BPA for an enrolled patient at a qualifying appointment.

Power Analysis

We expect at least 60,000 patients to be enrolled (at least 20,000 per arm). With this sample size, we will have 80% power to detect an increase in flu vaccination rates from 35% to 36.34% with two-tailed alpha = .05 for any comparison between arms.

Project Status

Patients were pre-randomized to their study arms in the summer of 2023. Patients are enrolled when they attend qualifying appointments where the BPAs fire. The study is ongoing through 4/1/23, when flu shot BPAs are turned off across the system.

Planned Analyses

Primary Outcome: *Patient received a flu vaccine (yes/no) [Time Frame: At the 1 day visit]*

Question 1: Do salient alerts indicating that patients are at high risk for flu and flu-related complications increase the likelihood that the patients will get vaccinated?

Analysis 1 (Confirmatory): We will test the hypothesis that patients whose clinicians were shown alerts with information about their risk status (patients randomized to the High-risk Alert or High-risk Alert with Risk Factors arms) will exhibit improved flu vaccination rates compared with patients in the Standard Alert arm.

For this analysis, we will run an OLS regression, including a binary predictor variable coding separately for baseline and the two High-risk Alert arms.

Question 2: Do alerts with information about a patient's factors that contribute to their high risk of flu and flu-related complications increase the likelihood that the patients will get vaccinated?

Analysis 2 (Exploratory): We hypothesize that patients whose providers were shown alerts with the factors that contributed to a patient's high risk (High-risk Alert with Risk Factors arm) will exhibit improved flu vaccination rates compared with patients in the arm with no risk factors (High-risk Alert arm).

For this analysis, we will run an OLS regression, including a binary predictor variable coding separately for each of the two High-risk Alert arms.

Analysis Notes

Analyses of the primary outcome will be limited to the first in-person appointment for each patient enrolled in the study. We will run a sensitivity analysis that includes patients who only attend telehealth appointments during the study.

Recent work suggests that OLS regressions are appropriate in randomized experiments with binary outcome variables such as ours (Gomila, 2021).

As the treatment variation is at the individual level, we will report heteroskedasticity-robust standard errors. We will also explore the impact of clustering these standard errors at the clinic and clinic-date levels to allow for dependence across observations within these clusters. We will also investigate heterogeneity across clinics that vary along characteristics of interest, including prior-year vaccination rates.

We may run additional robustness checks. These checks may include focusing on additional inclusion/exclusion criteria (e.g., including subsequent visits with alerts for a given patient) and subpopulations (e.g., different visit types).

Other Pre-specified Outcomes

Other Pre-specified Outcomes listed below include flu outcomes (diagnosis, complications) and COVID-19 vaccination. If there are any differences in these outcomes as a function of study

arm, the mechanism would almost certainly be increased flu vaccination. Therefore, we will only run analyses on Other Pre-specified Outcomes for analyses above where there is a significant difference in flu vaccination.

1. High confidence flu diagnosis

   Patient received a flu diagnosis via a positive polymerase chain reaction [PCR]/antigen/molecular test (yes/no) during the 2022-23 flu season (from the patient's appointment date through April 30, 2023)

   [Time Frame: Up to 8 months]

2. "Likely flu" diagnosis

   Received a "high confidence flu" diagnosis (with positive polymerase chain reaction [PCR]/antigen/molecular test) and/or "likely flu" diagnosis (as assessed via International Classification of Disease [ICD] codes or Tamiflu administration or positive PCR/antigen/molecular test) (yes/no) during the 2022-23 flu season (from the patient's appointment date through April 30, 2023)
   Note that "likely flu" is a superset of the "high confidence flu" diagnoses.

   [Time Frame: Up to 8 months]

3. Flu complications

   Diagnosed with flu-related complications (yes/no) during the 2022-23 flu season (from the patient's appointment date through April 30, 2023)

   [Time Frame: Up to 8 months]

4. ER visits

   Number of ER visits from the patient's message appointment date through July 31, 2023

   [Time Frame: Up to 11 months]

5. Hospitalizations

   Number of hospitalizations from the patient's message appointment date through July 31, 2023

   [Time Frame: Up to 11 months]

6. COVID-19 vaccination rates

   Received at least one COVID-19 vaccination (yes/no) during the 2022-23 flu season (from the patient's appointment date through April 30, 2023)

   [Time Frame: Up to 8 months]

7. Flu vaccination during the 2022-2023 season

Patient receives a flu vaccine (yes/no) during the 2022-23 flu season (from the patient's appointment date through April 30, 2023)

[Time Frame: Up to 8 months]

Additional Exploratory Analyses

1. Age and sex

   While older patients tend to be aware of their increased vulnerability, younger patients may be more surprised to learn of their high-risk status. Additionally, our previous work suggests that males and females are differentially likely to get vaccinated as a function of age, with younger females *more* likely to get vaccinated than males, and older females *less* likely to get vaccinated than older males.

   To test the relation between flu shots, age and sex, we will run an OLS regression including binned patient age (18–24, 25–34, 35–44, 45–54, 65+), sex, and their interaction.

   Additionally, we will test for an interaction between age, sex, and study arm, as people of different ages and sexes may be differentially receptive to different alert versions.

   We may also test whether alert effectiveness varies by clinician age and/or sex.

2. Risk level

   We will explore heterogeneity in flu vaccination rates within the top 20% of risk and test whether effects of study arm vary as a function of risk level.

3. Number of appointments

   Patients may have more than one appointment scheduled during the study where the flu BPA fired. We will explore whether vaccination rates were higher with more appointments for those in the experimental groups compared to those in the control group with the same number of appointments.

4. Appointment department/specialty

   Some departments give more flu shots than others. We will test if the alert versions are differentially effective as a function of department or specialty, to see if some versions are particularly helpful for under-performing departments or specialties.

5. Contamination analysis

   Although randomization was at the patient level, the intervention was directly experienced by clinicians rather than patients. Many clinicians encountered patients and their assigned BPAs for all three experimental arms. We will explore whether contamination was present in our data due to clinicians' exposure to multiple experimental conditions (e.g., by examining results as a function of clinic-level variation

in the number of patients randomly assigned to each arm and/or as a function of the duration of exposure to the information).