GENERAL INFORMATION
Alerts with Risk Information to Increase Influenza Vaccinations

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BACKGROUND AND OBJECTIVES
On average, 8% of the US population gets sick from the flu each flu season (Tokars et al. 2018). Since 2010, the annual disease burden of influenza has included 9-45 million illnesses, 140,000-810,000 hospitalizations, and 12,000-61,000 deaths (CDC 2020). The CDC 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 (CDC 2019). Flu vaccination is especially important during the COVID-19 pandemic, to minimize flu/COVID-19 coinfections and conserve healthcare resources.

One barrier to vaccination is a lack of “cues to action,” and, in particular, the lack of direct recommendation from medical personnel (Schmid et al. 2017); this barrier is arguably the 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. Nudges that increase clinician actions to recommend and order flu shots for their patients may therefore increase vaccinations more than attempts to nudge patients directly (e.g., by sending them text messages). Interruptive or “hard stop” alerts can help promote behavior that improves patient outcomes (Powers et al., 2018). And mechanisms that make an alert more salient can increase attention to a nudge and thus encourage action (Patel et al., 2017; Kim et al. 2017). These nudges are likely to be most effective when timely, for instance, as alerts to clinicians during those appointments (Milkman et al. 2021). In the 2020–21 flu season, Geisinger implemented a standard electronic health record (EHR) alert notifying clinicians when any outpatient they are seeing is eligible for a flu shot; yet, despite this alert, only a minority of patients are presently being vaccinated, especially at specialty appointments.

While most recover from influenza without treatment, the elderly, those with comorbidities, and other high-risk individuals can experience complications such as pneumonia, other respiratory illness, and death (Rothberg et al., 2008; Turner et al., 2003; WHO, 2010). Geisinger, a large health system in Pennsylvania, has partnered with Medial EarlySign (Medial; www.earlysign.com) to develop a machine learning (ML) algorithm to identify patients at risk for serious (moderate to severe) flu-associated complications based on existing EHR data. As part of our recent Roybal-funded pilots, Geisinger deployed this system during the 2020–21 and 2021–22 flu seasons and sent patients in the top 10% of predicted risk special messages (in addition to standard health system efforts) encouraging vaccination. Interim data from both pilots reveal that notifying patients about their high-risk status increases vaccination, but vaccination is not further increased by informing patients of how their risk was determined (Shermohammed et al., 2021) or by informing them of contributing risk factors from their medical records (Rosenbaum et al., 2021). Compared with patients, clinicians may be more receptive to information about individual patient risk factors, given their better understanding of medical diagnoses contributing to flu risk.

The present study will test the effectiveness of a clinician-facing nudge (e.g., salient, risk-based alert vs. a standard alert) on flu vaccination. This study builds on previous work supporting the effectiveness of salient alerts in encouraging flu vaccination (Kim et al., 2018; Patel et al., 2017) and extends it by focusing on alerts for people at high risk for flu and flu complications.

Specific Aims
Evaluate via randomized controlled trial the efficacy of a clinician-facing, EHR alert-based nudge promoting flu shots, alerting clinicians to their patients' high-risk status (with or without personalized contributing factors).

PROCEDURES
Research Design
Patients from the high-risk sample (primary target population) will be randomly assigned to one of at least two study arms. If necessary, we will randomize at the clinician or clinic level. Outcomes during the 2022–2023 flu season will be compared between study arms.

Study Population
1) Patients
Inclusion Criteria:
- Age 18+
- Have been determined to be in the top 20% of risk through Medial's ML algorithm
- Attend an appointment where the flu alert fires (Geisinger sets when flu alerts start and ends--between ~9/1/2022 and ~4/30/2023, as well as the trigger conditions for the alert, which includes valid departments and visits and excludes contraindications like Guillain-Barre syndrome)

2) Clinicians
Inclusion Criteria:
- Any Geisinger clinician who sees patient-participants in our study for an appointment where their flu shot alert fires

Recruitment and Enrollment
All patients will be recruited and enrolled from Geisinger; Massachusetts Institute of Technology (MIT)/National Bureau of Economic Research (NBER) collaborators will not be involved in recruitment or enrollment. Patients meeting the primary target population criteria will be enrolled into one of the experimental conditions. Anticipated enrollment number for this primary target population is 90,000. Only Geisinger clinicians for this primary target population will see the salient, risk-based alert for patients who were randomized to trigger it. Clinicians of patients who are not part of the study population will still see the standard flu alert if their patients are eligible for it as part of Geisinger's standard of care.

Detailed Study Procedures

Patients in the top 20% of risk for flu and flu complications based on the Medial EarlySign flu algomarker will be randomized to trigger a standard flu alert (specifically, a best practice alert) or a salient, specialized alert for clinicians throughout the 2022–23 flu season, stating the patients' level of risk (e.g., top 3%, top 10%, or top 20%). Among those who triggered the high-risk alert, we may further randomize this group to be shown or not shown the top factors contributing to patients' risk, based on Medial's algorithm. The high-risk alert will also include

text and color features to make the alert stand out among other alerts. Additionally, the high-risk alerts will be given priority, such that they are displayed above other unprioritized alerts (they will still show below high-priority alerts). The precise language and look of the alerts may change slightly from the attached drafts, as we are working with multiple teams at Geisinger, but the drafts are representative of the types of alerts that will be shown.

Geisinger introduces flu-related alerts on September 1st. As part of the research planning, randomization will occur in June 2022, in order to provide enough time to import risk scores and high-risk factors into Epic, so these data can be used to trigger the proper alerts. Because this intervention is timed to the 2022–23 flu season, the intervention period will begin ~9/1/22.

The primary outcome will be flu vaccination at the scheduled appointment, as recorded in the Geisinger EHR. We may limit the timeframe of the primary outcome to end earlier in the flu season (e.g., December), based on data suggesting that most patients get their flu shot by the end of the calendar year. If we choose this timeframe, we will still examine all data collected throughout the flu season. Additional outcomes to be measured between the patient's appointment and the end of the flu season will include: rates of flu diagnoses (both using the most rigorous biological tests, "high confidence flu", and using broader criteria that also include diagnosis codes and treatment information, "likely flu"), flu complications, and rates of other relevant healthcare utilization outcomes such as ER visits and hospitalizations. Finally, we will measure rates of COVID-19 vaccination in targeted patients.

Data Sources

All patients in this study will be in the top 20% of risk according to scores given by the Medial EarlySign flu algomarker. The development of this algorithm was already approved through a separate Geisinger IRB application (IRB number 2020-0211). Additionally, Geisinger deployed this system in a field study during the 2020–21 (IRB number 2020-0290) and 2021–22 flu seasons (IRB number 2021-0483) and contacted the identified patients with special messages (in addition to standard interventions conducted by the health system every flu season) to encourage vaccination.

In order to generate flu risk scores, Medial EarlySign has access to a de-identified, retrospective dataset in Geisinger's research environment. This environment is accessed by Medial EarlySign staff who have undergone appropriate training and are credentialed per Geisinger's research and Information Security/Access policies. This environment is protected by Geisinger Information Security Office standards that allow remote access to the Geisinger network in a 'sandbox'. All data and analysis are conducted within the secure environment and data do not leave the Geisinger network. The dataset contains EHR information on all patients who had a primary care encounter at Geisinger (outpatient or telemedicine) between 10/1/2008 and 4/13/2022.

Medial uses the retrospective dataset to generate flu risk scores for patients in that dataset who meet the following criteria:

1. Were born in the year 2004 or later (i.e., those turning 18 in the year 2022 and older)
2. Were alive according to the EHR as of April 2022 when the dataset was last updated
3. Either:
    a. Currently have a Geisinger PCP assigned
    b. Have been in the EHR since at least September 2021 AND have had at least one encounter in 2020–2022

After we obtain the base sample list from Medial, **Business Intelligence & Advanced Analytics** (BIAA), working with **Geisinger's Phenomics and Clinical Data Core** (PACDC), will pull a dataset to help us determine who meets our inclusion criteria and aid in NIH demographics reporting. This dataset will include demographic information, including patient birth date, race, ethnicity, and gender and/or sex. Finally, the dataset will include death date to ensure patients are living as of the date the data are extracted.

We will also obtain individual-level employee demographic information including age, gender, race, and ethnicity for provider-participants to aid in NIH demographics reporting. This information will be deidentified and aggregated prior to any external reporting or data sharing.

After the intervention is complete, we will obtain experimental outcome data for all population groups from BIAA & PACDC. This will include data on patient flu vaccination, diagnosis of flu, diagnosis of flu-like symptoms, presence of flu-associated complications, hospital visits, emergency department visits, and COVID-19 vaccination status. This dataset will additionally include patient characteristics that can serve as analysis covariates, such as: patient primary care provider and flu-related behavior and outcomes during previous flu seasons.

We may also request claims data from the Geisinger Health Plan (GHP; e.g., for claims related to flu vaccination, diagnosis, and complications). GHP claims data will be pulled by BIAA or the GHP data team (Pending approval from Research Contracts).

STUDY DATA DETAILS

Data Management Procedures and Confidentiality

The complete, identified study data will be accessed only by a Geisinger data broker and by limited Geisinger investigators with appropriate training and a legitimate need to know (i.e., Geisinger Co-Is and PIs), and any appropriately trained Geisinger staff, (e.g., clinicians, data analysts) who have a need to review the data for purposes of their normal Geisinger role.

A limited dataset containing dates of service and ZIP codes may be shared with any non-Geisinger collaborators (e.g., Additional Principal Investigator Doyle and his team) under a Data Use Agreement (pending approval) in compliance with HIPAA's Privacy Rule and using data security protocols reviewed and approved by the Geisinger Security Office, Privacy Office, and Information Technology department.

All data will be electronic. Datasets with full identifying information will only be stored on Geisinger-managed, password-protected computers of the data brokers for the purpose of linking datasets from different sources.

Identifiable data gathered for this study will be retained for at least 3 years, as required by NIH policy, and will be deleted after 3 years or after analysis is complete. After the data have been fully analyzed, the deidentified dataset will be shared along with publications from this study. The deidentified data will not be destroyed or removed after any prespecified period of time has elapsed. We intend to permanently and securely archive the deidentified dataset at a research repository such as Open Science Framework (OSF) in order to be consistent with the best practices for open and reproducible science, as well as our obligation to the public as NIA-funded researchers.

All data analysis will be conducted by Gail Rosenbaum, Henri Santos, Amir Goren, or limited other Geisinger investigators with appropriate training, and our non-Geisinger Collaborators. We

will analyze the data using standard behavioral research analysis methods, including computing bivariate correlations, using generalized linear models, using non-parametric models for non-normally distributed data, and entering variables as independent predictors in regression models to attempt to predict desired outcomes.

RESEARCH ACTIVITIES AT OTHER SITES

Geisinger is the lead research team for this multi-site study. Massachusetts Institute of Technology (MIT) and National Bureau of Economic Research (NBER) study personnel are considered not considered engaged in human subject research. Research activities conducted at MIT and NBER will be limited to data analysis, using limited data, as described above. MIT and NBER will not be involved in study recruitment/enrollment or intervention administration.

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