GENERAL INFORMATION

Encouraging Flu Vaccination Among High-Risk Patients Identified by a Machine-Learning Model of Flu Complication Risk

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BACKGROUND AND OBJECTIVES

On average, 8% of the US population gets sick from 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 the 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 will be especially important for high-risk patients during the COVID-19 pandemic so that flu cases are reduced and resources conserved.

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. Geisinger 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 on the basis of their existing electronic health record (EHR) data. The development of this algorithm was already approved through a separate Geisinger IRB application (**IRB number 2020-0211**). Geisinger will deploy this system during the 2020-21 flu season and contact the identified patients with special messages (in addition to standard efforts made by the health system every flu season) to encourage vaccination.

However, there is little evidence about (a) whether informing patients they are at high risk makes them more likely to receive vaccination; (b) how patients react to being told their risk status is the result of an analysis of their health records; and (c) whether informing patients their risk status has been determined by an "algorithm," by "machine learning," and/or by "artificial intelligence" (AI) will increase or decrease their likelihood of getting vaccinated. This study will address these gaps in the literature, which are especially important in light of the anticipated future growth of AI/ML system use throughout healthcare.

Medial's algorithm is an example of how interoperable health information exchange (HIE)—the ability for health information technology to share patient data—can improve the efficiency and effectiveness of healthcare. However, patients may not appreciate these benefits or the fact that healthcare has become substantially more integrated and collaborative. A systematic review of patient privacy concerns about HIE found that 15-74% of patients expressed privacy concerns,

depending on the study, and concluded that patient perspectives remain poorly understood. A flu outreach message that explicitly references a review of patient medical records might backfire as patients react poorly to a sense they have lost control of their health records, even though in this case the use is intended to benefit their care.

There is conflicting evidence on how people respond to advice or information that comes from an algorithm or machine. Dietvorst et al. (2015) documented a pattern of "algorithm aversion," in which people choose inferior human over superior algorithmic forecasts, especially after they observed the algorithm make an error. In contrast, Logg et al. (2018) described "algorithm appreciation," in which people followed advice more when they thought it came from algorithms than when they thought it came from human beings. Finally, Bigman and Gray (2019) found aversion to algorithms that make "moral decisions," including a (fictitious) medical decision of choosing whether or not to operate on a high-risk patient. In this study, the algorithm is merely advising patients on taking a low-risk action (an annual flu shot) that is already the standard of care and heavily encouraged by Geisinger for all patients (except, of course, those for whom the vaccine is contraindicated), and there is no opportunity to observe an erroneous recommendation, so the hypothesis is that "algorithm appreciation" will cause people to react positively to being informed of the algorithm's role. Thus, this study will address two important research questions:

1. Does informing patients that they are at high risk for flu complications (a) increase the likelihood that they will receive flu vaccine; and (b) decrease the likelihood that they receive diagnoses of flu and/or flu-like symptoms in the ensuing flu season?
2. Does informing patients that their high-risk status was determined (a) by analyzing their medical records (vs. by no specified method); and (b) by an AI/ML algorithm[1] analyzing their medical records (as opposed to via unspecified methods or human medical records analysis) affect the likelihood that they receive the flu vaccine and/or diagnoses of flu and/or flu-like symptoms in the ensuing flu season?

Our specific aims are:

1. Evaluate the effect on flu vaccination rates of informing health-system patients who are identified by an ML analysis of EHR data to be at high-risk for flu complications that they are at high risk with either (a) no additional explanation, (b) an explanation that this determination comes from an analysis of their medical records, and (c) the additional explanation that an AI or ML algorithm made this determination.
2. Evaluate the effects of the same three interventions on diagnoses of flu in the same patients.

[1] The study will not necessarily use the terms "AI," "ML," or "algorithm" in the messages; instead, these messages will be designed to be readable and comprehensible by the patient audience while still including the key concepts that differentiate the interventions from one another.

PROCEDURES

Research Design

Patients from the high-risk sample (primary target population) will be randomly assigned to one of 4 study arms. Outcomes during the 2020-2021 flu season will be compared between study arms.

Study Population

There are 3 separate populations to consider in the current study: the primary target population that will be randomized into an experimental condition and potentially contacted, and two secondary populations who will not experience an intervention and will only be included for data analysis purposes.

1) Primary target population

Inclusion Criteria:

- Aged 17 or older
- Have been determined as high-risk through Medial's ML algorithm

Exclusion Criteria:

- Has contraindications for flu vaccination
- Note: we will respect opt-out communication preferences, but will include patients in the study if they haven't opted out of at least one communication modality employed

2) Secondary population A (data analysis only): Household members

Inclusion Criteria:

- Household members of primary target population
- Have data in Geisinger's electronic health records

3) Secondary population B (data analysis only): Sub-threshold risk

Inclusion Criteria:

- Same as primary target population, except that these patients' algorithmic risk scores fall just below the high-risk cutoff

Exclusion Criteria:

- Same as primary target population

Recruitment and Enrollment. All patients meeting the primary target population criteria will be enrolled into one of the 4 experimental conditions. Anticipated enrollment number for this primary target population is 56,000. Only patients from this primary target population will be contacted. However, health record data will be accessed to assess secondary outcomes for household members of this target population (expected N of 234,000) and for patients whose risk scores were calculated by Medial's ML algorithm and determined to fall just below the high-risk cutoff (expected N of 56,000). This brings the total planned enrollment to 346,000 participants.

Detailed Study Procedures.

Eligible patients will be randomly assigned to one of 4 experimental conditions:

1. **Control**: In this condition, patients will receive no additional pro-vaccination intervention beyond Geisinger's normal efforts. Note that these efforts include a variety of Marketing and other system campaigns designed to encourage all patients and members to get their flu shot. In addition, the care gaps team has an annual campaign to encourage flu shots that targets patients who are determined by a non-ML assessment that they are at high risk for complications and we expect there to be overlap between this group of patients and the ML high-risk group we will be contacting. (Because the care gap team's high-risk patients are not told that they are at high risk or that they have been targeted, we are not concerned that this ongoing campaign will interfere with our ability to measure the effects of high-risk communication.)
2. **High Risk Only**: In this condition, patients will receive messages telling them they are at high risk for flu complications without specifying how/why Geisinger believes this to be the case.
3. **High Risk Based on Medical Record**s: In this condition, patients will receive messages telling them they have been identified to be at high risk for flu complications via analysis or review of their medical records. This is an accurate statement, since it does not specify that a human conducted this review or analysis. However, we anticipate that most readers will assume it was a human rather than an algorithm, allowing us to compare attitudes towards human versus machine risk determination.
4. **High Risk Based on Algorithm**: In this condition, patients will receive messages telling them they have been identified to be at high risk for flu complications via analysis of their medical records by AI/ML.

Because this intervention is timed to the 2020–21 flu season, the intervention period will begin ~9/1/20 and last for three months. During that period, all identified primary target population participants will be randomized and will receive 1–3 separate messages (content based on their assigned condition) in sequence via postal letter, SMS, and patient portal modalities, using all modalities available for each participant. Outcomes will be measured as of 5/31/21. Data extraction from the EHR, data cleaning, data analysis, and manuscript preparation will begin on or after 6/1/21 and will include data from not only the primary target population but also the two secondary populations.

The primary study outcomes will be the rates of flu vaccination and flu diagnoses during the 2020–21 season (start of intervention through 5/31/21) by the primary target population. We will also measure secondary, exploratory outcomes: Rates of flu vaccination and diagnoses by fellow household members of targeted patients; rates of flu vaccination and diagnoses by non-targeted patients who were assigned a risk score that fell just below the cutoff of targeted patients; rates of flu complications and flu-like symptoms among targeted patients, household members, and those at sub-threshold risk; and rates of other relevant healthcare utilization outcomes such as ER visits and hospitalizations.

Data Sources

In order to identify patients in the primary target population, **Business Intelligence & Advanced Analytics** (BIAA), working with **Geisinger's Phenomics and Clinical Data Core** (PACDC), will provide a list of patients (including patient identifiers such as Medical Record Number) that were assessed by the Medial and each patient's associated risks.

We will also obtain contact information (address, phone number, email address) to message participants in the primary target population from BIAA & PACDC.

After the intervention is complete, we will obtain experimental outcome data for all 3 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, and emergency department visits. This data set will additionally include patient characteristics that will be useful as analysis covariates, such as: age, patient primary care provider, and flu-related behavior and outcomes during previous flu seasons.

STUDY DATA DETAILS

Data Management Procedures and Confidentiality. All data will be electronic. Datasets with identifying information will only be stored on Geisinger-managed, password-protected computers of the data brokers (Amir Goren, Henri Santos, and Gail Rosenbaum) for the purpose of linking datasets from different sources.

A limited data set containing dates of service and ZIP codes will be shared with any non-Geisinger collaborators (e.g., Additional Principal Investigator Doyle and his team) under a Data Use Agreement 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.

After all data have been linked in a de-identified, coded file and analyzed, the datasets with identifiable information and any codes needed to link the identifiable information will be deleted. After the de-identified data have been fully analyzed, the de-identified 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.

The only study team members who will have access to identifiable and protected health information will be the data brokers: Amir Goren, Henri Santos, and Gail Rosenbaum. Our non-Geisinger collaborators will have access to a limited data set which includes de-identified data as well as dates of flu vaccination and diagnosis. The remaining investigators will have access to the de-identified, coded data during data analysis.

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, single IRB study. Massachusetts Institute of Technology (MIT) and National Bureau of Economic Research (NBER) will cede to Geisinger's IRB. Research activities conducted at MIT and NBER will be limited to data analysis, using limited data and de-identified data, as described above. MIT and NBER will not be involved in study recruitment/enrollment or intervention administration.

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