Full Study Protocol

GENERAL INFORMATION

Using AI Risk Predictions to Nudge Flu Vaccination

Christopher Chabris, Ph.D.

cfchabris@geisinger.edu

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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**). Additionally, Geisinger deployed this system in a field study during the 2020–21 flu season (**IRB number 2020-0290)** and contacted the identified patients with special messages (in addition to standard interventions conducted by the health system every flu season) to encourage vaccination. Geisinger will again deploy this system during the 2021-22 flu season.

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 our field experiment from the 2020-21 flu season, we found evidence of neither aversion nor appreciation: High-risk patients obtained vaccination at similar rates whether they were told their risk was determined by a computer algorithm or simply a review of their medical records (Shermohammed et al., 2021). At the same time, informing these patients about their risk status caused an increase and acceleration in flu vaccination compared with a care-as-usual control group. This suggests that informing patients about their risk status can be effective, but it is not evident that the increased vaccination rate went beyond what would have occurred with a flu vaccination message devoid of risk information. Therefore, the present study includes an active control message that encourages flu vaccination without revealing risk. The prior work varied the general description of how risk was identified, but it did not identify specific, personalized factors contributing to risk for individual patients. Providing such information increases the transparency, quantity, and prominence of risk factors, and it can build trust in the messages and their source. But it may also backfire, if patients have difficulty perceiving sensible connections between the explanations and the risk determination (Miller, 2019; Stubbs et al., 2007; Mercado et al., 2016). Next season's high-risk messages will include personalized risk factors identified as having the greatest predictive utility for patients' risk scores generated by the Medial ML model. The extent to which such explanatory information contributes to algorithm appreciation or aversion remains an open question.

Our specific aims are:

1. Evaluate whether providing influenza risk information to high-risk patients has a larger effect on vaccination rates than simple reminders (with no risk information).
2. Evaluate whether providing an explanation of the personalized factors that contributed to risk assessment specifically boosts vaccination.
3. Evaluate whether providing an explanation of the personalized factors that contributed to risk assessment results in aversion (as revealed in decreased vaccination) or appreciation (increased vaccination) of algorithm-based assessment, relative to a simple review of medical records.

PROCEDURES

Research Design

Patients from the high-risk sample (primary target population) will be randomly assigned to one of 5 study arms. Outcomes during the 2021-2022 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 18 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 will be recruited and enrolled from Geisinger; MIT/NBER collaborators will not be involved in recruitment or enrollment. Patients meeting the primary target population criteria will be enrolled into one of the 5 experimental conditions. Anticipated enrollment number for this primary target population is 47,000. 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 47,000). This brings the total planned enrollment to 346,000 participants.

Detailed Study Procedures.

Eligible patients will be randomly assigned to one of 5 experimental conditions:

1. **No-Contact 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 Gaps 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. **Reminder Control**: In this condition, patients will receive messages reminding them to get the flu shot without being advised of their risk status.
3. **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.
4. **High Risk Based on Medical Records:** 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, and they will be given one or more contributing risk factors from their medical record. 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.
5. **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, and they will be given one or more contributing risk factors from their medical record.

Risk factors includes in messages for Arms 4 and 5 may vary in their level of specificity. Some factors may be *specific*, in that they mention a particular medical function or process (e.g. "medical condition(s) or procedure(s) related to breathing"). Other factors may be *general*, without mentioning the medical function or process (e.g. "medical condition(s) or procedure(s)"). We may test whether outcomes vary as a function of factor specificity. We

included examples of specific and general messages in this protocol, along with a dictionary of all factors that may be included in messages.

In the 2020–21 study, messages were signed "Your Geisinger Health Team." In the present 2021–22 study, messages may be signed by the individual's PCP of record or by a clinical leader.

The copy for risk messages is nearly identical to messages sent during the 2020-2021 flu season (**IRB number 2020-0290)** with 2 main differences: 1) explanatory factors are added to messages for patients in Arms 4 and 5, and 2) the messages are written as if from a PCP rather than a team (e.g., "We are writing…" was changed to "I am writing…").

Because this intervention is timed to the 2021–22 flu season, the intervention period will begin ~9/1/21. Subjects in treatment Arms #2–5 will receive the same type of communication via up to three modalities—printed letters to their mailing addresses, SMS to their mobile phones, and/or secure messages via Geisinger's patient portal—depending on what consent and information is on file for each patient. Messages will be staggered by modality, starting with postal letters, then sending the same message via the patient portal two weeks later, and a final message via SMS after four weeks.

The primary outcome will be whether the patient was vaccinated during the first six weeks after the intervention begins. A secondary outcome will be vaccination within three months after the intervention begins. Additional secondary outcomes to be measured through the end of the flu season (start of intervention through 3/31/22) 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, hospitalizations, insurance claims (for an expected ~40% of participants who are members of Geisinger Health Plan) by patients, household members of patients, and those at sub-threshold risk. We will also measure rates of flu vaccination by fellow household members of targeted patients and non-targeted patients at sub-threshold risk. Finally, we will measure rates of COVID-19 vaccination in targeted patients, household members, and those at sub-threshold risk.

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,

emergency department visits, and covid vaccination status. 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 full identifying information will only be stored on Geisinger-managed, password-protected computers of the data brokers (Gail Rosenbaum and Amir Goren) 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 (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.

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 fully identifiable and protected health information will be Gail Rosenbaum and Amir Goren. Non-Geisinger collaborators will have access to a limited data set containing dates of service and ZIP codes. The remaining investigators will have access to the de-identified, coded data during data analysis.

All data analysis will be conducted by Gail Rosenbaum, Amir Goren 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, 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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