Personal and social patterns predict influenza vaccination decision

CURRENT STATUS: UNDER REVIEW

BMC Public Health  BMC Series

Adir Shaham
Tel Aviv University

Gabriel Chodick
Maccabi Healthcare Services

Varda Shalev
Maccabi Healthcare Services

Dan Yamin  dan.yamin@gmail.com
Tel Aviv University
Corresponding Author

DOI: 10.21203/rs.2.18839/v1

SUBJECT AREAS  Health Policy  Infectious Diseases

KEYWORDS
Influenza, Influenza vaccination, vaccination coverage, vaccine refusal, prediction
Abstract

Background

Seasonal influenza vaccination coverage remains suboptimal in most developed countries, despite longstanding recommendations of public health organizations. The individual’s decision regarding vaccination is located at the core of non-adherence. We analyzed large-scale data to identify personal and social behavioral patterns for influenza vaccination uptake, and develop a model to predict vaccination decision of individuals in an upcoming influenza season.

Methods

We analyzed primary data from the electronic medical records of a retrospective cohort of 250,000 individuals between the years 2007 and 2017, collected from 137 clinics. Individuals were randomly sampled from the database of Maccabi Healthcare Services. Maccabi’s clients are representative of the Israeli population, reflect all demographic, ethnic, and socioeconomic groups and levels. We used several machine-learning models to predict whether a patient would get vaccinated in the future. Models’ performance was evaluated based on the area under the ROC curve.

Results

The vaccination decision of an individual can be explained in two dimensions, personal and social. The personal dimension is strongly shaped by a “default” behavior, such as vaccination timing in previous seasons and general health consumption, but can also be affected by temporal factors such as respiratory illness in the prior year. In the social dimension, a patient is more likely to become vaccinated in a given season if at least one member of his family also became vaccinated in the same season. Vaccination uptake was highly assertive with age,
socio-economic score, and geographic location. An XGBoost-based predictive model achieved an ROC AUC score of 0.91 with an accuracy and recall rates of 90% on the test set. Prediction relied mainly on the patient’s individual and household vaccination status in the past, age, number of encounters with the healthcare system, number of prescribed medications, and indicators of chronic illnesses.

Conclusions

Our ability to make an excellent prediction of the patient’s decision sets a major step toward personalized influenza vaccination campaigns, and will help shape the next generation of targeted vaccination efforts.

Background

Influenza continues to constitute a major health threat with a significant economic burden. In the United States alone, influenza is estimated to cause over 100,000 hospitalizations and over 4,000 deaths each year \(^1\textsuperscript{-4}\). Similar outcomes are observed in most developed countries, including in Israel \(^5\textsuperscript{,6}\). The most efficient way for an individual to prevent influenza infection and its complications is vaccination \(^7\). Because influenza is an infectious disease, vaccination also reduces the transmission of influenza, providing benefits for both the vaccinated individual and the rest of the population \(^8\). Long-standing CDC recommendations suggest that all individuals above six months of age \(^9\) should be vaccinated against seasonal influenza. However, the majority of the US population does not comply with these recommendations, and vaccination rates against seasonal influenza hover around 40% annually \(^1\textsuperscript{0}\). Similar trends are observed in almost all developed countries \(^1\textsuperscript{1}\). Because the elderly above 65 are at higher risk of developing complications due to
influenza, the World Health Assembly has set a less ambitious goal of 75% vaccination coverage for this specific population\textsuperscript{12}. To encourage this goal, the OECD defined the vaccination coverage for the elderly as an important healthcare quality indicator. Nevertheless, the vast majority of developed countries fail to meet this goal.

The dissonance between the importance of influenza vaccination and the observed vaccination rates suggests that more research is required to understand the individual decision of whether or not to become vaccinated. Health behavior models, such as the Health Belief Model\textsuperscript{13}, place subjective and psychological elements at the core of the individual’s health behaviors. According to these models, the decision to vaccinate is often based on personal beliefs regarding vaccinations as well as an individual’s risk perceptions, which reflect the perceived severity of influenza, an individual’s perceived susceptibility, the perceived vaccination efficiency, and the effects of worries and regrets\textsuperscript{14–16}. Studies that rely on these models have two main methodological limitations: a) they are mostly based on small-scale and relatively homogeneous samples, and b) they were primarily derived from self-reported and subjective measurements that may lead to inherent biases. Furthermore, most of these studies did not take into account personal characteristics and behavioral patterns to predict future vaccination behavior.

Other studies in the field have analyzed large-scale data from social media and other sources. While some of these studies have focused on forecasting cases of illness\textsuperscript{17}, others aimed to capture the geographic and demographic patterns of influenza vaccination behavior relying on aggregated, rather than personal, vaccination data\textsuperscript{18}. Although electronic medical records (EMRs) are increasingly
used in research\textsuperscript{19}, even for predictive modeling\textsuperscript{20,21}, the usage of EMRs for influenza vaccination behavior remains limited. We sought to take advantage of EMRs and demographic data at large scale to address this gap in the literature. To our knowledge, this is the first study to analyze and predict decisions of individuals to get vaccinated against influenza using personal, detailed, and longitudinal data.

The goals of this study were to: a) Identify personal and social behavioral patterns and indicators for influenza vaccination uptake, and b) use these indicators to develop a machine-learning model that would predict vaccination decision of individuals in the upcoming influenza season.

Methods

Data Description and Case Definition

We analyzed primary data from anonymized electronic medical records of 250,000 individuals between the years 2007 and 2017, collected from Maccabi Healthcare Services (Maccabi). Maccabi is the second-largest health maintenance organization (HMO) in Israel, serving about 25\% of the population (2,215,000 clients). Maccabi’s clients are representative of the Israeli population, and reflect all demographic, ethnic, and socioeconomic groups and levels\textsuperscript{22}.

In order to avoid biases that may arise from death or changes in healthcare provider, we randomly selected 250,000 individuals who were members of Maccabi during the entire period from 2007 to 2017 or who were born during this period and remained members until 2017. We chose 2008 as the earliest influenza season because it was the first season that the vaccination was offered free of charge for all members of all the health-care providers in Israel\textsuperscript{23}. 

5
For each member, we compiled demographic characteristics, influenza vaccination history, respiratory diagnoses, prescriptions, encounters with the healthcare system, hospitalizations, chronic illnesses, and family connections to other members in the data set (SI Appendix, Table S1). The data were approved for use by Maccabi’s sub-Helsinki institutional review board, signed by Dr. Yosef Azuri, protocol number 0048-17-BBL.

**Season:** Influenza is a seasonal disease, with the highest prevalence between October and March\(^ {24}\). Therefore, we defined each “season” as the period ranging from June 1 until May 31 of the following year and named it after the end year. For example, “season 2016” was defined as the period between June 1, 2015 and May 31, 2016.

**Age group:** We divided the population into the seven age groups (0-4, 5-16, 17-25, 26-35, 36-50, 51-64, and 65+). This division was done with respect to the season in question; if a specific analysis included several seasons, the population was divided into age groups separately in each season. Therefore, in some cases, a patient belonged to one age group in a specific season and moved to another age group in the following season.

**Respiratory Illness:** We define a respiratory illness as a respiratory diagnosis reported by a physician, according to several codes from the International Statistical Classification of Diseases and Related Health Problems protocol (ICD-9; SI Appendix Table S2). These diagnoses need not necessarily be confirmed by a lab, because we are interested in perception rather than the reality.

**Family:** Family members are defined as a set of patients having the same “family code” in the surveillance systems of Maccabi. Among the 250,000 patients included in our study, 55,749 patients shared a “family code” with at least one other patient.
within the data, creating 25,999 families.

To accomplish the two goals of this study, we established three discrete steps. The first step was *personal pattern analysis*, in which we identified behavioral patterns that relate to the personal aspects of an individual’s vaccination decision. The second step was *social pattern analysis*, in which we evaluated the environmental factors that may influence an individual’s vaccination decision. Finally, in the *predictive modeling step*, we developed a machine learning model that converted the data and the insights from the previous tasks into an individual-level prediction of a future vaccination decision. The third step was conducted in accordance with the tripod statement\(^{25}\) for multivariable prediction models.

### A. Descriptive personal patterns

We examined the behavior of a random variable representing the probability of a patient to become vaccinated in a given season, as a function of the patient’s vaccination decision and respiratory illnesses in the previous season. For each season (among the 2009-2017 seasons), we divided the population into seven age groups and then divided each age group into four mutually exclusive sub-groups: 1) patients who vaccinated and became infected in the previous season, 2) patients who vaccinated and did not become infected in the previous season, 3) patients who were not vaccinated and became infected in the previous season, and 4) patients who were not vaccinated and did not become infected in the previous season. We calculated the proportion of patients who became vaccinated in the given season for each of the 28 groups.

We then created a measurement that encodes the time during the season that each patient became vaccinated, and named it the patient’s *Average Vaccination Rank*. In each season, each patient received a value within the range [0 - 1], representing
the timing of the vaccination within the season relative to other patients. The first patient to become vaccinated received the value 1, and the last patient to become vaccinated received the value 0. The patient’s Average Vaccination Rank was defined as the average of these values across seasons the patient became vaccinated in. In order to examine the distribution of the Average Vaccination Ranks among patients, we divided the population into 11 mutually exclusive groups according to the number of vaccinations in a 10-season period. For this purpose, we excluded patients under 10 years old. We then used boxplot analysis to depict the distribution of the Average Vaccination Rank among each group separately by age groups.

We also examined the relationship between healthcare consumption and vaccination decision. We used two measurements for this purpose: 1) the average number of prescribed medications (of any kind) per season, and 2) the vaccination proportion, calculated as the number of seasons that the patient became vaccinated out of 10 seasons, or less for patients under 10. We then divided the population into 10 equal groups by deciles of the average number of prescriptions and examined the distribution of the vaccination proportion for each group separately using boxplot analysis. In addition, we conducted a similar analysis for the average number of encounters with the healthcare system (of any kind).

B. Descriptive Social patterns

Family analysis – we analyzed the vaccination decision of patients with respect to the vaccination decisions of other members of the patients’ families. We then calculated a relative risk for becoming vaccinated, defining the exposed group as the group of patients with at least one other family member who became vaccinated in a given season. This analysis was conducted for all seasons combined. We also
examined the similarities between family members over time and compared it to the similarities between randomly sampled patients (SI Appendix Figure S1).

**Geographic analysis** - Each patient was associated with one of 137 Maccabi clinics, where he receives most of his medical care. We used the vaccination proportion, calculated as the number of seasons the patient became vaccinated out of 10 seasons (or less for patients under 10) and grouped the patients by clinic. We then conducted an ANOVA test to examine the variance between clinics. In addition, we calculated the proportion of patients who became vaccinated, for each season, at each clinic. We then took all 3,070 statistical areas in Israel (according to the Israeli Central Bureau of Statistics) and associated each statistical area with its nearest clinic. Using these data, we created a heat-map that displays the variance in vaccination proportion across socioeconomic areas based on the average vaccination proportion across all seasons in the associated clinics.

**Socioeconomic analysis** - We performed an analysis of the vaccination proportion with respect to the socioeconomic score, range from 1 to 10, that was assigned to each patient by Maccabi. We calculated the average vaccination proportion for each socioeconomic score across all seasons and displayed the variance of the vaccination proportion of different socioeconomic scores.

C. **Predictive modeling**

We developed a model to predict the influenza vaccination behavior of a patient in a future influenza season. The predictive model development was guided by and made in accordance with the tripod statement\(^ \text{25} \) for multivariable prediction models. This is a classification problem with a binary label, as the patient may or may not become vaccinated (positive label or negative label, respectively). We created a time-free model, which does not attempt to predict a patient’s behavior in a specific
season, but rather allows predicting behavior in any future season given the relevant previous data. Based on the results of an entropy analysis (SI Appendix), we used the data of three consecutive seasons in order to predict the behavior in the subsequent fourth season. For example, we data from seasons 2008 through 2010 to predict each patient’s behavior in 2011, data from seasons 2009 through 2011 were used to predict behavior in 2012, and so on. Therefore, the ten-season period data of each patient produced up to seven records with seven labels (seasons 2011 - 2017), depending on the patient’s age, creating a dataset of 1,553,907 records in total.

The features we used for the prediction were based on demographic attributes of the patient and on calculated or aggregated medical characteristics. In order to build a comprehensive model, the features of the dataset were rather basic. Because 55,749 of the patients had family members within the data, we could extract family-related features in addition to the basic features. We therefore divided the 1,553,907 records into 2 datasets: a basic dataset containing 1,225,032 records, where each record had 27 features and a label, and a ‘family’ dataset containing 328,875 records, where each record had 30 features and a label. The features are described under Sociodemographic & EMR in Table 1 (a detailed description can be found in Table S3 in the SI Appendix).

We trained several models using the following algorithms: 1) Logistic Regression26, 2) Naïve Bayes26, 3) XGBoost Random Forest27, 4) Light GBM Random Forest28 and 5) Artificial Neural Network26. While preprocessing, we used min-max scaling where relevant. Random Forest algorithms were trained using 500 decision trees. We split both the basic dataset and the family dataset into training sets (70%),
validation sets (15%), and test sets (15%). We trained each algorithm on both train sets, creating two models, one for each dataset (basic dataset and family dataset), using 4-fold cross-validation to maximize the ROC AUC score. When training the models, we conducted hyper-parameters tuning using grid-search to discover the combination of parameters that performed best on the train set. Detailed description of the hyper-parameters tuning is presented in (Table S4).

After the training phase, we received two trained models for each algorithm. We predicted the labels of the records in the validation sets and evaluated the performance of the models using the ROC AUC score, precision, recall, and F1-score. As a benchmark, we created four additional simple models. The first is the Age model and it relies on the patient’s age alone. The second one is the Sociodemographic model (SD), which does not utilize personal medical records, but instead uses a subset of demographic features of the patient and the vaccination coverage in the patient’s clinic. The third is Vaccination decision in the previous season model (PS), which relies solely on the patient’s behavior in the previous season; this model predicts that an individual that became vaccinated in the last season will become vaccinated in the predicted season, and vice versa. The fourth simple model, the Vaccination decision in the previous season & Sociodemographic model (PS&SD), uses the patient’s behavior in the previous season in addition to the features used by SD model. The features of the models are described in Table 1.

Because none of the simple models use family-based features, they were all trained over the entire training population and predicted the labels for all validation samples. The training of these simple models was based solely on the algorithm that performed best on the basic and family datasets.

Finally, we evaluated the most successful models and the simple models on the test
sets, and analyzed the feature importance of these models.

Results

Overall, we found several personal and social behavioral patterns that are associated with a patient's tendency to become vaccinated and that provide predictive insight into the future vaccination decision of the patient. Furthermore, these patterns served as the foundations for a machine learning modeling phase, which yielded an accurate and comprehensive predictive model for the patient's vaccination decision in the next season.

A. Descriptive personal patterns

The average seasonal vaccination coverage is approximately 20%. Of the 250,000 patients included in this study, 101,407 (41%) became vaccinated at least once, 32,584 (13%) became vaccinated at least five times, and only 7,609 (3%) became vaccinated during this entire 10-year period. The age of the patients in 2017, ranged from 1 year to 116 years, with a median of 36 years (first quartile = 12 years, third quartile = 53 years). Fifty-two percent of the patients were female.

By examining the decision of a patient to become vaccinated in a given season with respect to the patient’s vaccination decision and respiratory diagnosis in the season prior, we found two main patterns: 1) The default effect – a patient is much more likely to become vaccinated if she or he has done so in the previous season; 2) Patients who were not vaccinated in the previous season and were also diagnosed with respiratory illness were more likely to become vaccinated in the next season (Figure 1A). We further found that the more frequently a patient becomes vaccinated, the higher the patient’s Average Vaccination Rank, meaning that the patient tends to become vaccinated in an earlier stage of the season. These findings
were consistent in all age groups (Figure 1B).

Finally, both the average number of prescriptions and the average number of encounters with the healthcare system are associated with vaccination proportion. Patients that scored higher on these metrics (i.e., those with more prescriptions and more interactions with the healthcare system) are also characterized by higher values of vaccination proportion (Figure 2).

B. Descriptive - Social Patterns

By analyzing the vaccination decision of patients with respect to the vaccination decisions of their family members, we found that a patient is 11.09 times more likely to become vaccinated in a given season, if at least one member of his or her family also became vaccinated in the same season (RR: 11.09; 95% CI: 10.92 to 11.25). Our geographic analysis revealed significant differences between different clinics (P value <.0001), with average vaccination rates ranging between 4.4% and 25.3%. A geographical heat map of the average vaccination rates displays these differences among the statistical areas of Israel (Figure 3A). In addition, we observed that a higher socioeconomic score is associated with a higher vaccination rate (Figure 3B).

C. Predictive modeling

In the basic datasets (train, validation and test), the age of the patients, as of 2017, ranged from 3 years to 116 years, with a median of 43 years (first quartile = 19 years, third quartile = 58 years). Fifty-two percent of the patients were female. In the family datasets (training, validation, and test), the age of the patients in 2017 ranged from 3 years to 94 years, with a median of 17 years (first quartile = 11 years, third quartile = 45 years). Fifty-three percent of patients in the family
datasets were female.

We evaluated all models using the precision, recall, F1 score and ROC AUC measurements (SI Appendix, Table S4). The most successful models, which utilize sociodemographic and EMR data, were the XGBoost and LightGBM algorithms, with an ROC AUC score of 0.91 on the basic validation and test sets and 0.88 on the family validation and test sets. Although the XGBoost achieved slightly better F1-scores, we found that while the XGBoost holds a higher precision than the LightGBM for positive-label records (i.e., individuals who became vaccinated), its recall among these records is relatively lower. These differences may arise from the differences between the two algorithms\textsuperscript{28}, which create different decision forests and therefore different predictions.

All four simple models – Age, Sociodemographic (SD), Vaccination decision in the previous season (PS), and Vaccination decision in the previous season & Sociodemographic (PS&SD) achieved lower scores than did the XGBoost algorithm in all measurements. The PS&SD model was the most successful of the four, with an ROC AUC score of 0.87 on the validation and test sets. An ROC AUC comparison of the four simple models and the XGBoost, which was the most successful model of those utilizing sociodemographic & EMR data, is shown in Figure 4.

According to a feature importance analysis for both the XGBoost and LightGBM models, the patient’s previous vaccination decisions are the most prominent features in the algorithms’ prediction process. When data were available, the vaccination decisions of a patient’s family also played a meaningful role in prediction. These features were followed by other personal features such as the patient’s age, the number of encounters with the healthcare system, the number of prescribed medications and chronic illnesses. The five most prominent features in
the algorithms’ prediction process of the XGBoost model, the LightGBM model, and the simple models (except the Age model) are presented in Table 2. An elaborated feature importance plots is presented in figure S2.

Discussion

From a large-scale analysis of electronic medical records and demographic data, we identified several behavioral patterns regarding influenza vaccination and developed a machine-learning model that predicts the decision making of the individual in the next season. Our results indicate that the vaccination decision of an individual can be explained in two dimensions – personal and social. The personal dimension is strongly shaped by a “default” behavioral approach, which is often manifested in repeated vaccination decisions in subsequent seasons, a preferred timing of vaccination within the season. This approach is associated with a patient’s healthcare consumption measurements. We also found evidence that this “default” behavior could be affected by temporal effects such as a recent respiratory illness diagnosis, suggesting that experiencing a recent respiratory illness changes patients’ perception of the risk associated with influenza. The social dimension can be divided into the social environment and immediate relatives. We observed significant differences in vaccination rates in different geographical regions and in patients with different socioeconomic scores. We also observed that family members tended to have similar vaccination decisions. It is likely that while the social environment sets a general approach towards influenza vaccination as a context, immediate relatives may influence the ad-hoc decision of an individual. These patterns served as a foundation for our predictive machine learning models, which take advantage of the EMR data and demographic data to provide an
excellent prediction of an individual’s future vaccination decision. Previous vaccination decisions, along with age, number of encounters with the healthcare system, and prescriptions, serve as the strongest predictors of a future vaccination decision. In cases where the family vaccination decision in previous seasons is provided, it also serves as a strong predictor. The simple models demonstrate how a fine prediction can be made even when only a small subset of the patient’s personal and social information is available.

The behavioral patterns that we observed by analyzing the Israeli population are consistent with widely held hypotheses regarding individual decision making in several key ways. First, our work corroborates the importance of previous vaccination decisions and the influence of an individual’s social circle in predicting the future decisions. However, our study extends these behavioral concepts by using large-scale longitudinal data and objective measurements. In spite of the inherent differences between cultures and healthcare systems worldwide, we believe that the behavioral patterns and the predictive models we have developed can be reproduced with rather minor modifications in most developed countries.

This study identifies and relies on correlations and associations, in both pattern analysis and predictive modeling, and does not attempt to assume or imply causality. In addition, this study does not explicitly account for intervention efforts by Maccabi during the study period or any possible effects of media exposure. Furthermore, the collected data do not contain information of vaccinations programs in workplaces, which are relatively effective in Israel, and yet small-scale. Despite these limitations and in light of the fact that most individuals do not become vaccinated on a seasonal basis, our ability to make an excellent prediction of an
patient’s decision-making represents a major step towards personalized influenza vaccination campaigns. In this way, our work can help shape the next generation of targeted and customized vaccination efforts. Our study demonstrates how personal EMRs and demographic data can give new insight into a patient’s perceptions and can serve as a platform to anticipate the most likely decision of an individual. This predictive capacity will likely be valuable for healthcare providers and health insurance agencies who may wish to design intervention effort for their patients or to assess the required number of doses of influenza vaccination.

Future research can bridge the gap between our probability-based prediction and intervention efforts, by creating customized intervention plans for individuals according to their predicted likelihood of becoming vaccinated and other personal characteristics, in order to optimize influenza vaccination uptake, particularly when facing resource constraints.

Conclusion

Influenza vaccination decision of an individual is highly predictable, and can be identified even in the absence of detailed medical information about the patient. Predictors primarily include vaccination timing in previous seasons and general health consumption, but can also be affected by temporal factors such as respiratory illness in the prior year. Other predictors include vaccination uptake of family members and vaccination coverage in the individual’s main clinic in the year prior as well as standard socio-demographic characteristics. Our ability to make an excellent prediction of the patient’s decision sets a major step toward personalized influenza vaccination campaigns against vaccine refusales, and will help shape the next generation of targeted vaccination efforts.
Abbreviations

ROC: Receiver operating characteristic; AUC: Area under the Curve; EMR: Electronic Medical Record; RR: Relative risk.

Declarations

Acknowledgements

We thank Adi Rennert from Maccabitech for all the administrative work required for the IRB approval. We also like to thank Matan Yehezkel from for his contribution to the design of the study, and Angelika Hofmann for her help in editing the manuscript.

Authors’ Contributions

DY and AS contributed to the study design, analysis and interpretation of the results. GH and VS contributed in providing and interpreting the raw data. AS and DY wrote the first draft of the manuscript. All authors contributed to further versions of the manuscript. All authors have read and approved the manuscript.

Funding

This research was supported by the Koret Foundation grant for Smart Cities and Digital Living.

Availability of data and materials

The data that support the findings of this study are available from the Maccabi Health Services but restrictions apply to the availability of these data, which were used under license for the current study and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Maccabi Health Services.
Ethics approval and consent to participate

Ethics and study approval was conducted by the Helsinki institutional review board of “Maccabi Health Services” signed by Dr. Yosef Azuri protocol number 0048-17-BBL. Because the study was performed in accordance with the Israeli Public Health Code for public health purposes with anonymized data, there were no further requirements for ethical approval, consent to participate or data protection agency approval.

Consent for publication

Not Applicable

Competing interest

The authors declare that they have no competing interests.

References

1. Thompson WW, Shay DK, Weintraub E, et al. Influenza-associated hospitalizations in the United States. *J Am Med Assoc*. 2004. doi:10.1001/jama.292.11.1333.

2. Rolfes MA, Foppa IM, Garg S, et al. Annual estimates of the burden of seasonal influenza in the United States: A tool for strengthening influenza surveillance and preparedness. *Influenza Other Respi Viruses*. 2018. doi:10.1111/irv.12486.

3. Thompson, MG, Shay, DK, Zhou, H, Bridges, CB, Cheng, PY, Burns, E, Bresee, JS, Cox N. Estimates of deaths associated with seasonal influenza --- United States, 1976-2007. *MMWR Morb Mortal Wkly Rep*. 2010. doi:mm5933a1 [pii].

4. Reed C, Chaves SS, Daily Kirley P, et al. Estimating Influenza Disease Burden from Population-Based Surveillance Data in the United States. *PLoS One*. 2015;10(3):e0118369. doi:10.1371/journal.pone.0118369.
5. Preaud E, Durand L, Macabeo B, et al. Annual public health and economic benefits of seasonal influenza vaccination: A European estimate. *BMC Public Health*. 2014. doi:10.1186/1471-2458-14-813.

6. Yamin D, Gavious A, Davidovitch N, Pliskin JS. Role of intervention programs to increase influenza vaccination in Israel. *Isr J Health Policy Res*. 2014;3:13. doi:10.1186/2045-4015-3-13.

7. Nichol KL. The efficacy, effectiveness and cost-effectiveness of inactivated influenza virus vaccines. *Vaccine*. 2003;21(16):1769-1775. doi:10.1016/S0264-410X(03)00070-7.

8. Ghendon Y. Influenza: its impact and control. *World Heal Stat Q*. 1992;45(2-3):306-311. http://www.ncbi.nlm.nih.gov/pubmed/1462665.

9. Grohskopf LA, Sokolow LZ, Broder KR, Walter EB, Fry AM, Jernigan DB. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices-United States, 2018-19 Influenza Season. *MMWR Recomm reports Morb Mortal Wkly report Recomm reports*. 2018;67(3):1-20. doi:10.15585/mmwr.rr6703a1.

10. Santibanez T, Kahn K, Zhai Y, et al. Flu Vaccination Coverage United States, 2015-16 Influenza Season. Center for Disease Control and Prevention.

11. Endrich MM, Blank PR, Szucs TD. Influenza vaccination uptake and socioeconomic determinants in 11 European countries. *Vaccine*. 2009. doi:10.1016/j.vaccine.2009.04.029.

12. OECD. *OECD (2015), “Influenza for Older People”, in Health at a Glance 2015: OECD Indicators*. OECD Publishing, Paris; 2015. doi:http://dx.doi.org/10.1787/health_glance-2015-57-en.

13. Rosenstock IM. Historical Origins of the Health Belief Model. *Health Educ*
14. Brewer NT, Chapman GB, Gibbons FX, Gerrard M, McCaul KD, Weinstein ND. Meta-analysis of the relationship between risk perception and health behavior: the example of vaccination. *Heal Psychol.* 2007. doi:10.1037/0278-6133.26.2.136.

15. Chapman GB, Coups EJ. Emotions and preventive health behavior: Worry, regret, and influenza vaccination. *Heal Psychol.* 2006. doi:10.1037/0278-6133.25.1.82.

16. Chapman GB, Coups EJ. Predictors of influenza vaccine acceptance among healthy adults. *Prev Med (Baltim).* 1999. doi:10.1006/pmed.1999.0535.

17. Santillana M, Nguyen AT, Dredze M, Paul MJ, Nsoesie EO, Brownstein JS. Combining Search, Social Media, and Traditional Data Sources to Improve Influenza Surveillance. *PLoS Comput Biol.* 2015. doi:10.1371/journal.pcbi.1004513.

18. Huang X, Smith MC, Paul MJ, et al. Examining Patterns of Influenza Vaccination in Social Media. *Work Thirty-First AAAI Conf Artif Intell.* 2017.

19. Goldstein BA, Navar AM, Pencina MJ, Ioannidis JPA. Opportunities and challenges in developing risk prediction models with electronic health records data: a systematic review. *J Am Med Informatics Assoc.* 2017. doi:10.1093/jamia/ocw042.

20. Miotto R, Li L, Kidd BA, Dudley JT. Deep Patient: An Unsupervised Representation to Predict the Future of Patients from the Electronic Health Records. *Sci Rep.* 2016. doi:10.1038/srep26094.

21. Wu J, Roy J, Stewart WF. Prediction modeling using EHR data: Challenges, strategies, and a comparison of machine learning approaches. *Med Care.* 2010.
22. Cohen R, Rabin G, National Insurance Institute R and PA. Membership in Sick Funds 2016 [Hebrew]. Period Surv 289. 2017:104. http://www.btl.gov.il.

23. Israel Ministry of Health. Influenza vaccination, Ministry of Health. Prevention of seasonal flu and other winter illnesses.

24. Bloom-Feshbach K, Alonso WJ, Charu V, et al. Latitudinal Variations in Seasonal Activity of Influenza and Respiratory Syncytial Virus (RSV): A Global Comparative Review. PLoS One. 2013. doi:10.1371/journal.pone.0054445.

25. Moons KGM, Altman DG, Reitsma JB, et al. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): Explanation and elaboration. Ann Intern Med. 2015. doi:10.7326/M14-0698.

26. Pedregosa F, Varoquaux G, Gramfort A, et al. Scikit-learn: Machine Learning in Python. J Mach Learn Res. 2012. doi:10.1007/s13398-014-0173-7.2.

27. XGBoost documentation.
http://xgboost.readthedocs.io/en/latest/parameter.html.

28. Ke G, Meng Q, Wang T, et al. LightGBM: A highly efficient gradient boosting decision tree. Adv Neural Inf Process Syst. 2017.

29. Shahrabani S, Benzion U. Workplace vaccination and other factors impacting influenza vaccination decision among employees in Israel. Int J Environ Res Public Health. 2010. doi:10.3390/ijerph7030853.

Tables

Table 1. Features of the models used in this study. “V” represents that a specific feature was used in a specific model.
| Feature(s)                                                                 | Socio demographic model | Vaccination decision in previous season model |
|---------------------------------------------------------------------------|-------------------------|----------------------------------------------|
| Age                                                                       | V                       |                                              |
| Gender                                                                    | V                       |                                              |
| Socioeconomic scores                                                     | V                       |                                              |
| Country of origin                                                         |                         |                                              |
| Year of immigration                                                       |                         |                                              |
| Vaccination indicator in the previous season                              | V                       |                                              |
| Vaccination rank in the three previous seasons                            |                         |                                              |
| Number of respiratory diagnoses in the three previous seasons             |                         |                                              |
| Cumulative hospitalized days in the three previous seasons (hospitalizations of any reason) |                         |                                              |
| Number of encounters with the healthcare system in the three previous seasons (encounters of any reason) |                         |                                              |
| Number of prescribed medications in the three previous seasons (any kind of medications) |                         |                                              |
| Chronic illness in the three previous seasons                             |                         |                                              |
| Vaccination proportion at the patient’s clinic, in the three previous seasons | V                       |                                              |
| Average Vaccination rank of the patient’s family in the three previous seasons |                         |                                              |

Table 2. Cumulative contributions of the ranked top five features to each model
| Feature's Rank | XGB model for the basic dataset (ROC AUC score: 0.91) | XGB model for the family dataset (ROC AUC score: 0.88) | LightGBM model for basic dataset (ROC AUC score: 0.91) | LightGBM model for family dataset (ROC AUC score: 0.88) | Socdem (RC) |
|----------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|----------|
| 1st            | Vaccination rank in the season prior (29%)      | Vaccination rank in the season prior (27%)      | Vaccination rank in the season prior (47%)      | Vaccination rank in the season prior (30%)      | Age      |
| 2nd            | Vaccination rank two seasons prior (51%)        | Vaccination rank two seasons prior (39%)        | Vaccination rank two seasons prior (69%)        | Average Vaccination rank of the patient's family in the season prior (51%) | Vac      |
| 3rd            | Vaccination rank three seasons prior (60%)      | Average Vaccination rank of the patient's family two seasons prior (45%) | Vaccination rank three seasons prior (81%)      | Vaccination rank two seasons prior (60%)        | Vac (80) |
| 4th            | Number of prescribed medications in the season prior (67%) | Average Vaccination rank of the patient's family in the season prior (49%) | Age (85%)                                       | Average Vaccination rank of the patient's family two seasons prior (66%) | Soc (1)  |
| 5th            | Chronic illness in the season prior (72%)       | Chronic illness two seasons prior (53%)         | Number of encounters with the healthcare system in the season prior (89%) | Age (70%)                                       | Vac (97) |

**Figures**
(A) Vaccination coverage in the 2017 season with respect to vaccination decision
Vaccination rate and healthcare consumption. Boxplot charts of the average vaccination rank by (A) the number of prescriptions per season (deciles) and (B) the number of encounters per season (deciles). The deciles values are displayed on the boxes.

Figure 3

(A) Geographical heat map of the average vaccination rates across season 2008-2017. The axes represent the number of vaccinations and the seasons as a function of socioeconomic score. The 95% confidence interval is displayed on top of each bar.
Figure 4

Receiver operating characteristic (ROC) curves comparison

Supplementary Files

This is a list of supplementary files associated with the primary manuscript. Click to download.

SI Appendix.docx

Declarations

Acknowledgements

We thank Adi Rennert from Maccabitech for all the administrative work required for the IRB approval. We also like to thank Matan Yehezkel from for his contribution to the design of the study, and Angelika Hofmann for her help in editing the manuscript.

Authors’ Contributions
DY and AS contributed to the study design, analysis and interpretation of the results. GH and VS contributed in providing and interpreting the raw data. AS and DY wrote the first draft of the manuscript. All authors contributed to further versions of the manuscript. All authors have read and approved the manuscript.

**Funding**

This research was supported by the Koret Foundation grant for Smart Cities and Digital Living.

**Availability of data and materials**

The data that support the findings of this study are available from the Maccabi Health Services but restrictions apply to the availability of these data, which were used under license for the current study and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Maccabi Health Services.

**Ethics approval and consent to participate**

Ethics and study approval was conducted by the Helsinki institutional review board of “Maccabi Health Services” signed by Dr. Yosef Azuri protocol number 0048-17-BBL. Because the study was performed in accordance with the Israeli Public Health Code for public health purposes with anonymized data, there were no further requirements for ethical approval, consent to participate or data protection agency approval.

**Consent for publication**

Not Applicable

**Competing interest**

The authors declare that they have no competing interests.

**References**

1. Thompson WW, Shay DK, Weintraub E, et al. Influenza-associated hospitalizations in the United States. *J Am Med Assoc.* 2004. doi:10.1001/jama.292.11.1333.
2. Rolfes MA, Foppa IM, Garg S, et al. Annual estimates of the burden of seasonal influenza in the United States: A tool for strengthening influenza surveillance and preparedness. *Influenza Other Respi Viruses*. 2018. doi:10.1111/irv.12486.

3. Thompson, MG, Shay, DK, Zhou, H, Bridges, CB, Cheng, PY, Burns, E, Bresee, JS, Cox N. Estimates of deaths associated with seasonal influenza --- United States, 1976-2007. *MMWR Morb Mortal Wkly Rep*. 2010. doi:mm5933a1 [pii].

4. Reed C, Chaves SS, Daily Kirley P, et al. Estimating Influenza Disease Burden from Population-Based Surveillance Data in the United States. *PLoS One*. 2015;10(3):e0118369. doi:10.1371/journal.pone.0118369.

5. Preaud E, Durand L, Macabeo B, et al. Annual public health and economic benefits of seasonal influenza vaccination: A European estimate. *BMC Public Health*. 2014. doi:10.1186/1471-2458-14-813.

6. Yamin D, Gavenous A, Davidovitch N, Pliskin JS. Role of intervention programs to increase influenza vaccination in Israel. *Isr J Health Policy Res*. 2014;3:13. doi:10.1186/2045-4015-3-13.

7. Nichol KL. The efficacy, effectiveness and cost-effectiveness of inactivated influenza virus vaccines. *Vaccine*. 2003;21(16):1769-1775. doi:10.1016/S0264-410X(03)00070-7.

8. Ghendon Y. Influenza: its impact and control. *World Heal Stat Q*. 1992;45(2-3):306-311. http://www.ncbi.nlm.nih.gov/pubmed/1462665.

9. Grohskopf LA, Sokolow LZ, Broder KR, Walter EB, Fry AM, Jernigan DB. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices-United States, 2018-19 Influenza Season. *MMWR Recomm reports Morb Mortal Wkly report Recomm reports*. 2018;67(3):1-20. doi:10.15585/mmwr.rr6703a1.

10. Santibanez T, Kahn K, Zhai Y, et al. Flu Vaccination Coverage United States, 2015-16
Influenza Season. Center for Disease Control and Prevention.

11. Endrich MM, Blank PR, Szucs TD. Influenza vaccination uptake and socioeconomic determinants in 11 European countries. *Vaccine*. 2009. doi:10.1016/j.vaccine.2009.04.029.

12. OECD. *OECD (2015), “Influenza for Older People”, in Health at a Glance 2015: OECD Indicators*. OECD Publishing, Paris; 2015. doi:http://dx.doi.org/10.1787/health_glance-2015-57-en.

13. Rosenstock IM. Historical Origins of the Health Belief Model. *Health Educ Monogr*. 1974. doi:10.1177/109019817400200403.

14. Brewer NT, Chapman GB, Gibbons FX, Gerrard M, McCaul KD, Weinstein ND. Meta-analysis of the relationship between risk perception and health behavior: the example of vaccination. *Heal Psychol*. 2007. doi:2007-03487-002 [pii]\r10.1037/0278-6133.26.2.136.

15. Chapman GB, Coups EJ. Emotions and preventive health behavior: Worry, regret, and influenza vaccination. *Heal Psychol*. 2006. doi:10.1037/0278-6133.25.1.82.

16. Chapman GB, Coups EJ. Predictors of influenza vaccine acceptance among healthy adults. *Prev Med (Baltim)*. 1999. doi:10.1006/pmed.1999.0535.

17. Santillana M, Nguyen AT, Dredze M, Paul MJ, Nsoesie EO, Brownstein JS. Combining Search, Social Media, and Traditional Data Sources to Improve Influenza Surveillance. *PLoS Comput Biol*. 2015. doi:10.1371/journal.pcbi.1004513.

18. Huang X, Smith MC, Paul MJ, et al. Examining Patterns of Influenza Vaccination in Social Media. *Work Thirty-First AAAI Conf Artif Intell*. 2017.

19. Goldstein BA, Navar AM, Pencina MJ, Ioannidis JPA. Opportunities and challenges in developing risk prediction models with electronic health records data: a systematic review. *J Am Med Informatics Assoc*. 2017. doi:10.1093/jamia/ocw042.

20. Miotto R, Li L, Kidd BA, Dudley JT. Deep Patient: An Unsupervised Representation to
Predict the Future of Patients from the Electronic Health Records. *Sci Rep.* 2016. doi:10.1038/srep26094.

21. Wu J, Roy J, Stewart WF. Prediction modeling using EHR data: Challenges, strategies, and a comparison of machine learning approaches. *Med Care.* 2010. doi:10.1097/MLR.0b013e3181de9e17.

22. Cohen R, Rabin G, National Insurance Institute R and PA. Membership in Sick Funds 2016 [Hebrew]. *Period Surv* 289. 2017:104. http://www.btl.gov.il.

23. Israel Ministry of Health. Influenza vaccination, Ministry of Health. Prevention of seasonal flu and other winter illnesses.

24. Bloom-Feshbach K, Alonso WJ, Charu V, et al. Latitudinal Variations in Seasonal Activity of Influenza and Respiratory Syncytial Virus (RSV): A Global Comparative Review. *PLoS One.* 2013. doi:10.1371/journal.pone.0054445.

25. Moons KGM, Altman DG, Reitsma JB, et al. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): Explanation and elaboration. *Ann Intern Med.* 2015. doi:10.7326/M14-0698.

26. Pedregosa F, Varoquaux G, Gramfort A, et al. Scikit-learn: Machine Learning in Python. *J Mach Learn Res.* 2012. doi:10.1007/s13398-014-0173-7.2.

27. XGBoost documentation. http://xgboost.readthedocs.io/en/latest/parameter.html.

28. Ke G, Meng Q, Wang T, et al. LightGBM: A highly efficient gradient boosting decision tree. *Adv Neural Inf Process Syst.* 2017.

29. Shahrabani S, Benzion U. Workplace vaccination and other factors impacting influenza vaccination decision among employees in Israel. *Int J Environ Res Public Health.* 2010. doi:10.3390/ijerph7030853.

Tables
Table 1. Features of the models used in this study. “V” represents that a specific feature was used in a specific model.

| Feature(s)                                                | Socio demographic model | Vaccination decision in the previous season model |
|-----------------------------------------------------------|-------------------------|--------------------------------------------------|
| Age                                                       | V                       |                                                  |
| Gender                                                    | V                       |                                                  |
| Socioeconomic scores                                     | V                       |                                                  |
| Country of origin                                         |                         |                                                  |
| Year of immigration                                       |                         |                                                  |
| Vaccination indicator in the previous season              |                         | V                                                |
| Vaccination rank in the three previous seasons            |                         |                                                  |
| Number of respiratory diagnoses in the three previous seasons |                     |                                                  |
| Cumulative hospitalized days in the three previous seasons (hospitalizations of any reason) |                         |                                                  |
| Number of encounters with the healthcare system in the three previous seasons (encounters of any reason) |                         |                                                  |
| Number of prescribed medications in the three previous seasons (any kind of medications) |                         |                                                  |
| Chronic illness in the three previous seasons             |                         |                                                  |
| Vaccination proportion at the patient’s clinic, in the three previous seasons |                         | V                                                |
| Average Vaccination rank of the patient’s family in the three previous seasons |                         |                                                  |

Table 2. Cumulative contributions of the ranked top five features to each model
| Feature's Rank | XGB model for the basic dataset (ROC AUC score: 0.91) | XGB model for the family dataset (ROC AUC score: 0.88) | LightGBM model for basic dataset (ROC AUC score: 0.91) | LightGBM model for family dataset (ROC AUC score: 0.88) | Socio-demographic (ROC AUC score: 0.77) |
|---------------|------------------------------------------------------|-------------------------------------------------------|------------------------------------------------------|-------------------------------------------------------|----------------------------------------|
| 1<sup>st</sup> | Vaccination rank in the season prior (29%)           | Vaccination rank in the season prior (27%)            | Vaccination rank in the season prior (47%)           | Vaccination rank in the season prior (30%)            | Age (67%)                              |
| 2<sup>nd</sup> | Vaccination rank two seasons prior (51%)             | Vaccination rank two seasons prior (39%)             | Vaccination rank two seasons prior (69%)             | Average Vaccination rank of the patient's family in the season prior (51%) | Vaccination at the patient's clinic, in the season prior (74%) |
| 3<sup>rd</sup> | Vaccination rank three seasons prior (60%)           | Average Vaccination rank of the patient's family two seasons prior (45%) | Vaccination rank three seasons prior (81%)           | Vaccination rank two seasons prior (60%)             | Vaccination at the patient's clinic, two seasons prior (80%) |
| 4<sup>th</sup> | Number of prescribed medications in the season prior (67%) | Average Vaccination rank of the patient's family in the season prior (49%) | Age (85%)                                           | Average Vaccination rank of the patient's family two seasons prior (66%) | Socioeconomic score (1) (87%)          |
| 5<sup>th</sup> | Chronic illness in the season prior (72%)            | Chronic illness two seasons prior (53%)              | Number of encounters with the healthcare system in the season prior (89%) | Age (70%)                                           | Vaccination at the patient's clinic, three seasons prior (97%) |

**Figures**
Figure 1

(A) Vaccination coverage in the 2017 season with respect to vaccination decision and respir
Figure 2

Vaccination rate and healthcare consumption. Boxplot charts of the average vaccination rank by (A) the number of prescriptions per season (deciles) and (B) the number of encounters per season (deciles). The deciles values are displayed on the boxes.

Figure 3

(A) Geographical heat map of the average vaccination rates across season 2008-2017. The geographical region is divided into 10 socioeconomic scores, with the highest scores indicating higher socio-economic status. (B) Bar chart showing vaccination coverage by socioeconomic score, with higher scores corresponding to higher vaccination rates.
Figure 4

Receiver operating characteristic (ROC) curves comparison

Supplementary Files

This is a list of supplementary files associated with the primary manuscript. Click to download.

SI Appendix.docx