The relative benefits of claims and electronic health record data for predicting medication adherence trajectory

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Background Healthcare providers are increasingly encouraged to improve their patients' adherence to chronic disease medications. Prediction of adherence can identify patients in need of intervention, but most prediction efforts have focused on claims data, which may be unavailable to providers. Electronic health records (EHR) are readily available and may provide richer information with which to predict adherence than is currently available through claims.

Methods In a linked database of complete Medicare Advantage claims and comprehensive EHR from a multi-specialty outpatient practice, we identified patients who filled a prescription for a statin, antihypertensive, or oral antidiabetic during 2011 to 2012. We followed patients to identify subsequent medication filling patterns and used group-based trajectory models to assign patients to adherence trajectories. We then identified potential predictors from both claims and EHR data and fit a series of models to evaluate the accuracy of each data source in predicting medication adherence.

Results Claims were highly predictive of patients in the worst adherence trajectory (C = 0.78), but EHR data also provided good predictions (C = 0.72). Among claims predictors, presence of a prior gap in filling of at least 6 days was by far the most influential predictor. In contrast, good predictions from EHR data required complex models with many variables.

Conclusion EHR data can provide good predictions of adherence trajectory and therefore may be useful for providers seeking to deploy resource-intensive interventions. However, prior adherence information derived from claims is most predictive, and can supplement EHR data when it is available. (Am Heart J 2018;197:153-62.)

Background

The epidemic of nonadherence to prescription medication is recognized as a substantive threat to the individual, population, and economic health of the United States.[1-5] Approximately 15% of patients do not fill a new prescription.[6] Of those who do fill the initial prescription, approximately one-half discontinue therapy in the first six months.[4,7-10] Nonadherence prevents patients from receiving the full benefit of prescription medications and is associated with adverse health outcomes and higher healthcare costs.[8-10] Many of the most effective interventions to improve adherence rely on a resource-intensive mix of strategies that simultaneously promote patient adherence and address the many potential barriers to adherence.[11-13] Predicting which patients are likely to become nonadherent can aid in targeting resource-intensive interventions to improve adherence to the patients most likely to benefit.

Efforts to predict adherence have received substantial attention from payers because they stand to reduce overall expenditures through better evidence-based medication use. These efforts have primarily relied on claims data, which is readily available to payers.[14] Payment reform has meant that providers are also increasingly interested in efforts to improve chronic disease management, and nonadherence is a major focus of attention in this context[15]; while providers have increasing access to claims data to undertake these activities, claims generally have a substantial delay and must be managed separately for each insurer. In contrast, providers have access to electronic health records (EHR), which are available to provider organizations for use in near real time and contain a wealth of structured and unstructured data that may provide much richer information with which to predict adherence than is currently available through claims.

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0002-8703

https://doi.org/10.1016/j.ahj.2017.09.019

Therefore, we sought to evaluate the accuracy of predictions of medication adherence based on EHR data versus claims. We utilize a unique dataset containing both complete healthcare claims and linked comprehensive outpatient EHR. We focus on predictors measurable in these data sources at the beginning of adherence assessment among both new initiators and prevalent users of therapy for 3 important chronic diseases: type II diabetes mellitus (T2DM), hypertension, and hyperlipidemia.

Methods

Data source and cohort

The study population consisted of Tufts Health Plan Medicare Advantage beneficiaries aged 65 and older, receiving care at Harvard Vanguard Medical Associates (HVMA), a multi-specialty medical group practice providing care to more than 530,000 adult and pediatric patients at more than 25 offices across eastern Massachusetts. For these patients, we obtained a de-identified, linked database of complete healthcare claims and HVMA EHR information during 2010 to 2012. Healthcare claims included enrollment files and medical and pharmacy claims, including claims generated outside HVMA. EHR data included structured variables, such as demographics, laboratory values, and appointment information. Adherence was assessed from pharmacy claims, while predictors of adherence were assessed using either claims or EHR data.

From these data, we identified patients who filled a prescription for a statin, anti-hypertensive, or oral anti-diabetic drug between January 2011 and September 2012 (listed in Appendix Table I). These medications were selected as they provide therapy for 3 of the most common chronic diseases and frequently co-occur. We defined the index date for each treatment episode as the date of the first observed prescription fill of a study drug during this time period, and patients could have up to one treatment episode in each therapeutic area. Patients were required to have continuous beneficiary enrollment in the year prior to the index date and were followed up for subsequent medication fills for a maximum of 360 days after the index date. Follow-up was censored in the event of disenrollment from the health insurer, a nursing home or hospice admission, or end of data availability (December 2012). Patients were excluded if they had fewer than 112 days of follow-up after the index date; this length was chosen because a patient receiving a 90-day supply on the index date requires 112 days to finish the supply with 80% adherence, thus ensuring that follow-up accurately assess the presence of at least one refill. The institutional review board of Brigham and Women's Hospital approved the study.

Adherence measurement

Adherence was assessed based on medication filling recorded in pharmacy claims. We used group based trajectory models to assign patients to groups with distinct longitudinal filling patterns. Since trajectory groups typically represent more homogeneous adherence behaviors than groups based on simple ratio or discontinuation metrics, they may provide adherence predictions that are more useful for targeting adherence interventions. In addition, past work has shown that trajectory groups are sometimes easier to predict than other adherence categories.[16]

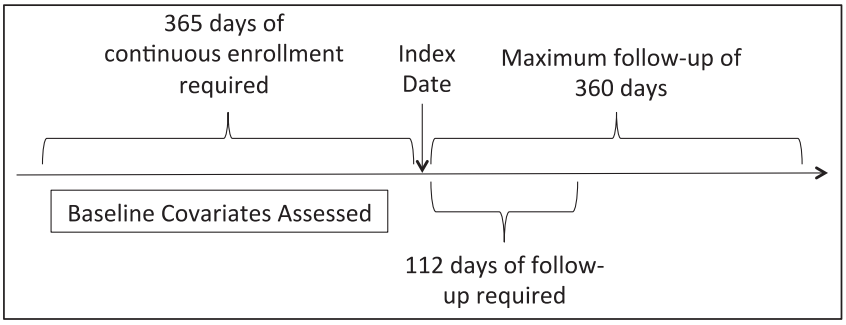
We first created a supply diary for each patient and each medication class that indicates whether each day of follow-up was covered with medication by linking all observed fills within the class based on the dispensing date and the days' supply. Each supply diary began at the first prescription within the class on or after the index date and continued to the end of follow-up. Based on the supply diaries, we calculated the proportion of days covered (PDC) during each 30-day period of follow-up for each medication class. The denominator was adjusted for the number of days of follow-up for each class and for days hospitalized during the period. We then labeled each month during follow-up as adherent or non-adherent based on the average PDC for all of a patient's medications within the therapeutic area during the period using the standard threshold of PDC $\geq$/$<$0.8. A PDC threshold of 80% is used by most quality measures to define good adherence,[14,17] and it corresponds to the level of use above which patients with coronary artery disease benefit from statins.[18] For patients with less than 360 days of follow-up, PDC was missing for some months (see Appendix Figure 1 for information on how the model assigns patients with incomplete data). Figure 1 depicts the study timeline.

We then modeled the 12 monthly indicators of adherence as a longitudinal response in a logistic group-based trajectory model (PROC TRAJ, a downloadable add-on package to SAS version 9.3, SAS Institute, Cary, NC). This model can accommodate patients who are missing adherence data in some months by using all available data to model adherence and assign patients to trajectory groups. As recommended, we considered multiple models varying the number of groups from 2 to 6. We selected the 5-group model as having the best fit because it had the lowest Bayesian Information Criterion (BIC) value, it assigned patients to groups with high probability (typically $>$0.9), and it resulted in trajectory groups that each had a substantial number of patients.[19,20] All models considered used third-order polynomials (linear, squared, and cubic terms) of time to model the probability of being adherent, as past work has shown that adherence trajectories over one year or longer are often highly non-linear.[16] On the basis of the selected model, we assigned patients to the trajectory group with the highest probability of membership.

Predictors of adherence

All predictors were assessed using data accrued during the 365 days prior to and including the index date. Predictors were selected on the basis of hypothesized contribution to prediction and the ability to be measured

Figure 1



Overview of study design.

at index among both new initiators and prevalent users of medications; therefore, there is minimal consideration of prior adherence, which typically cannot be measured in new users.

Demographics. Patient demographics, including age and sex, were available in both claims and EHR and were required to agree between the data sources for linkage. Thus, these variables could be derived from either data source. Additional area-level demographic information was derived from census data and used to supplement claims or EHR predictors, including median income, percent black race, and percent with a high-school diploma in the zip code of patient residence.

Claims-based predictors. We defined patient characteristics using claims, including a measure of burden of comorbidities using the combined comorbidity score; use of healthcare services such as office visits, emergency room visits and hospitalizations[21-24]; an indicator for a gap in medication supply of >6 days in the year prior to index date (among prevalent users); and features of the index prescription fill, such as whether it was for a branded or generic medication, the number of remaining refills, and an indicator for >30 days' supply.

EHR-based predictors. EHR variables were defined to replicate potential predictors that would otherwise only be available through claims. For example, number of refills remaining at index and an indicator for a prior gap in medication coverage were constructed based on medication orders in the EHR. In addition, other variables that are not available in claims were derived, including patient ethnicity and language, clinical laboratory values, and patient communications with providers. For example, structured fields include information on patient smoking status, alcohol use, body mass index (BMI), and laboratory results. For patients who did not have any available measurements of pulse, blood pressure (BP), low-density lipoprotein (LDL) cholesterol, or HbA1c, we imputed the patient's value using the mean value from all patients in the relevant therapeutic area. Missing BMI was considered to be a separate BMI category.

Prediction models

The prediction models were estimated using the generalized boosting algorithm, as implemented in the R package gbm.[25] The boosting algorithm has been used frequently in health care research from administrative databases[26,27] and is considered one of the best data-mining approaches for general prediction problems.[28,29] In this analysis, we constructed several multinomial models predicting trajectory group using multiple different data source combinations as the source of predictors, including: (1) Demographics alone; (2) Demographics + Claims alone; (3) Demographics + EHR alone, (4) Demographics + Claims + EHR. Demographics are included in all models, since they could be derived from either claims or EHR data alone.

Evaluation of prediction models

Prediction models were evaluated with respect to their ability to discriminate between patients who did and did not become non-adherent, as measured by the C-statistic. A C-statistic can be interpreted as the probability that for any pair of randomly chosen cases and controls (adherent and non-adherent patients) the predicted probability from the model will be higher for the case than for the control.[30] This measure ranges from 0.5 to 1.0, corresponding to a completely non-informative model (a case has a 50% chance of having a higher predicted probability than a randomly selected control) and perfect prediction, respectively. The practical meaning of a model C-statistic depends on how the predictions are used, but a model with higher C-statistic will generally lead to more accurate patient targeting, for example, a higher sensitivity and specificity when labeling patients as likely adherent or not. In general, $C \geq 0.7$ is considered to represent a good model and $C \geq 0.8$ represents a strong model.[31]

To avoid the "over optimism" bias associated with evaluating model prediction accuracy in the same data that was used to estimate the model, we performed 10-fold cross-validation (CV).[32] In this method, the cohort was

randomly partitioned into 10 samples of approximately equal size. The first sample was set aside, and the remaining nine were used for model estimation. The estimated model was then applied to patients from the first sample (that were excluded from model estimation) to generate predictions. This process was repeated for each of the 10 samples until every patient had a single prediction that was generated without the use of his data in model estimation. These predictions were then compared with the relevant adherence measure to calculate a single C-statistic. The statistical significance of differences in predictive accuracy across models was assessed via tests of the net reclassification index (NRI).[33]

Prediction rules

Because C-statistics and the difference in C-statistics do not provide simple clinical interpretations, we selected a small subset of variables that were highly influential based on the variable importance measure from the boosted models. We then used these variables to construct simple prediction rules for identifying patients likely to be in the best adherence trajectory (group 1) or the worst trajectory (group 5). We similarly created rules using the CV predicted probabilities from the claims alone model and the EHR alone models. For these models, we selected patients that had a predicted probability in the top 10% for the given trajectory group as likely to be in that group. For each potential rule, we calculated the proportion of patients predicted to be in the trajectory, the positive predictive value (PPV), and the negative predictive value (NPV). For comparison, we also calculated statistics for the "No information" rule, which assumes all patients will be in the trajectory of interest.

This work was funded by Merck Sharp and Dohme, Inc. The research contract granted Brigham and Women's Hospital right to publication of results as well as final wording of the manuscript.

The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the manuscript, and its final contents.

Results

Patient characteristics

We identified 19,841 treatment episodes from 11,479 patients meeting all inclusion criteria, including 7,783 patients filling a statin, 10,122 filling an anti-hypertensive, and 1936 filling an anti-diabetic (Appendix Table II). The mean follow-up was 345 days. The baseline characteristics of patients at the start of each treatment episode are presented in Table I. The average age was 76 years, and the cohort included 43% males. Area-level socioeconomic status was high, as the median income was $86,203 and 91% of residents had at least a high school diploma, on average.

As measured from claims, use of generic drugs and long index prescriptions (≥90 days' supply) was high, but a large proportion had a prior gap in medication use (67%). These variables were also independently measured using EHR fields. Although the overall means or prevalences of many characteristics were similar whether measured from claims or EHR, the correlations between the claims variables and the corresponding EHR variables were often poor (Table I). For example, the number of refills remaining and the indicator of a prior gap had correlations between claims and EHR measurements of −0.15 (95% confidence interval [CI] -0.14, −0.16) and 0.06 (0.05, 0.07), respectively.

Additional variables measured from the EHR showed that approximately half of the patients reported being married or living with a companion. More than 95% had at least one blood pressure and pulse measurement in the baseline period, slightly fewer had at least one BMI measurement, and more than 75% had at least one LDL cholesterol measurement. Although not shown in the table, 45% of statin patients, 40% of antihypertensive patients, and 85% of antidiabetic patients had at least one measurement of all relevant variables. On average, LDL and Hb_{A1c} levels were in the range of clinical control when available. More than 25% of patients did not show up for at least one appointment in the year prior to index.

Predicting adherence trajectory using claims

We selected the 5-group trajectory model for categorizing patients' adherence patterns. These trajectories are presented in Figure 2, and include patients who (1) had almost perfect adherence during follow-up; (2) filled regularly during the first 9 months, and then discontinued; (3) filled sporadically throughout the 12 months; (4) discontinued after 6 months of follow-up; and (5) had a rapid decline in medication use shortly after the index fill. Comparison of the trajectory groupings with 12-month PDC as well as comparisons of drug-specific versus overall trajectory groupings is provided in Appendix Tables III–IV and Appendix Figure 2.

The CV C-statistic from each model predicting trajectory group membership is presented in Table II. When predicting adherence using claims, accuracy was highest to predict membership in Trajectory 5 (worst adherence group) with a C-statistic of 0.78, indicating moderately high accuracy. When predicting other trajectories, C-statistics ranged from 0.58 to 0.67. Plots of the relative influence of each variable used in the models to predict all five trajectories simultaneously (Figure 3) show that the strongest claims-based predictors were prior gaps in adherence, length of the index fill, and number of available refills.

Predicting adherence trajectory using EHR

EHR data alone also provided moderately good prediction accuracy for Trajectory 5 (C = 0.72), and poor to moderate accuracy for other trajectories (0.55-0.62). Prediction from EHR data relied on a wider set of predictors than prediction from claims, including length of index

Table I. Mean (standard deviation) or percent prevalence of patient characteristics measured from claims or EHR

Patient characteristics	Claims	EHR	Correlation*
Demographics			
Age	76 (5.4)	76 (5.4)	
Male sex	42.7%	42.7%	
% Black in zip code	6.9 (12.4)	6.9 (12.4)	
% High school diploma in zip code	91.4 (6.0)	91.4 (6.0)	
Median income in zip code	$86,204	$86,204	
Medication and comorbidities			
Combined comorbidity score	1.0 (2.3)	0.7 (1.9)	0.80 (0.80, 0.81)
Length of index fill >30 days	71.4%	68.2%	0.66 (0.65, 0.66)
Daily Dosage >1x	15.7%	13.3%	0.66 (0.65, 0.66)
Number of available refills	1.7 (2.0)	2.4 (3.0)	−0.15 (−0.16, −0.14)
Gap >6 days for index medication	70.9%	80.6%	0.06 (0.05, 0.07)
Number of unique meds	8.9 (4.8)	9.5 (6.5)	0.85 (0.84, 0.85)
Number of unique anti-hypertensive meds	2.2 (1.3)	2.0 (1.3)	0.89 (0.89, 0.90)
Number of unique statins meds	0.8 (0.4)	0.8 (0.4)	0.82 (0.82, 0.82)
Number of unique anti-diabetic meds	0.4 (0.6)	0.4 (0.6)	0.94 (0.94, 0.95)
Hospitalization	17.4%	32.1%	0.61 (0.60, 0.62)
ER visit	13.9%	16.2%	0.69 (0.67, 0.70)
Number of physician visits	25.5 (26.0)	5.7 (4.5)	0.43 (0.41, 0.44)
Number of unique providers	12.2 (9,1)	13.8 (11.5)	0.45 (0.43, 0.46)
Index medication is generic	92.2%		
Additional demographics			
Single or living alone		36.0%	
Married or living Together		49.4%	
Black or African American		6.0%	
English as primary language		90.9%	
Lab values			
At least one systolic BP measurement		97.2%	
Average systolic BP in mmHg		129.1 (11.2)	
At least one pulse measurement		95.6%	
Average pulse in beats per minute		68.0 (5.0)	
At least one BMI measurement		93.0%	
Most recent BMI value		21.7%	
At least one LDL measurement		80.3%	
Most recent LDL value in mg/dL		94.0 (27.6)	
At least one HbA1c measurement		52.7%	
Most recent HbA1c value in mmol/L		6.6 (0.6)	
Other			
Number of immunizations		0.9 (0.9)	
No show for at least one appointment		25.8%	
Number of phone calls per patient		13.9 (18.4)	

For variables measured in both, correlations with 95% confidence intervals are provided.
*Correlations for demographic variables were 1.0, since these variables were required to agree for linkage.

medication order, calculated number of available fills, recent LDL, patient language, number of phone calls made by the patient to the practice site, and having at least one missed appointment. Some of these variables that contain many potential categories, such as patient language, are likely subject to some overfitting, thereby overestimating their influence in prediction.

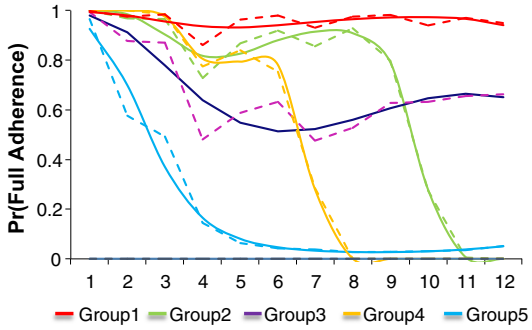
Added value of both claims and EHR

Models that used all available information, including both claims and EHR, performed similarly to models that contained claims predictors alone, and both models had consistently higher C-statistics than models that used only EHR information. These differences in predictive accuracy between the full model and the model using EHR data alone were all statistically significant as assessed via the net reclassification index (see Appendix Table II), indicating that claims add meaningful improvement in prediction beyond that available with EHR alone, despite moderately good performance with EHR alone.

Prediction rules

Table III presents PPV and NPV of select prediction rules from the claims and EHR data to predict whether patients will have sustained good adherence over the following year (Trajectory 1) or are likely to soon decline in adherence (Trajectory 5). If the goal is to identify patients who do not need intervention, then we seek

Figure 2



Observed and predicted proportion of patients adherent each month after index in each of 5 groups identified by the trajectory model. Solid and dashed curves represent estimated and observed monthly adherence prevalence, respectively.

Table II. Predictive ability of models predicting membership in each trajectory group using cross-validated C-statistics*

Trajectory	Demographics	Demographics + claims	Demographics + EHR	Demographics + claims + EHR
1 (N = 1396)	0.54 (0.53, 0.55)	0.67 (0.66, 0.68)	0.62 (0.61, 0.62)	0.68 (0.67, 0.69)
2 (N = 3936)	0.53 (0.51, 0.55)	0.58 (0.56, 0.59)	0.55 (0.54, 0.57)	0.57 (0.56, 0.59)
3 (N = 2008)	0.53 (0.52, 0.54)	0.62 (0.61, 0.62)	0.55 (0.54, 0.56)	0.62 (0.61, 0.63)
4 (N = 801)	0.52 (0.50, 0.54)	0.58 (0.57, 0.60)	0.57 (0.55, 0.59)	0.60 (0.58, 0.61)
5 (N = 11,700)	0.54 (0.53, 0.55)	0.78 (0.77, 0.79)	0.72 (0.71, 0.73)	0.79 (0.78, 0.80)

*C ≥ 0.7 is considered to represent a good model and C ≥ 0.8 represents a strong model.

rules for predicting Trajectory 1 with high PPV to ensure that few patients who need intervention are assigned to this group. Trajectory 1 was the most common trajectory (57%), and this prevalence value serves as the baseline PPV for the no information rule that predicts that all patients will be in trajectory 1. When using claims data, restricting to patients without a prior gap in medication supply of >6 days improves the PPV considerably (77%), and further restricting to patients with a long index fill supply and at least 4 remaining refills provides little improvement (82%). Using the model provides similar PPV (81.7%) with slightly better NPV.

When using EHR data alone to predict Trajectory 1, all 6 of the best predictors were needed to construct a rule that reached a PPV of 66%. In contrast, the model using all EHR data performed better (70%), but resulted in slightly decreased NPV. Interestingly, having fewer available refills, as measured in the EHR, was associated with a slightly higher probability of being in the best trajectory, despite a reverse association when measured in claims.

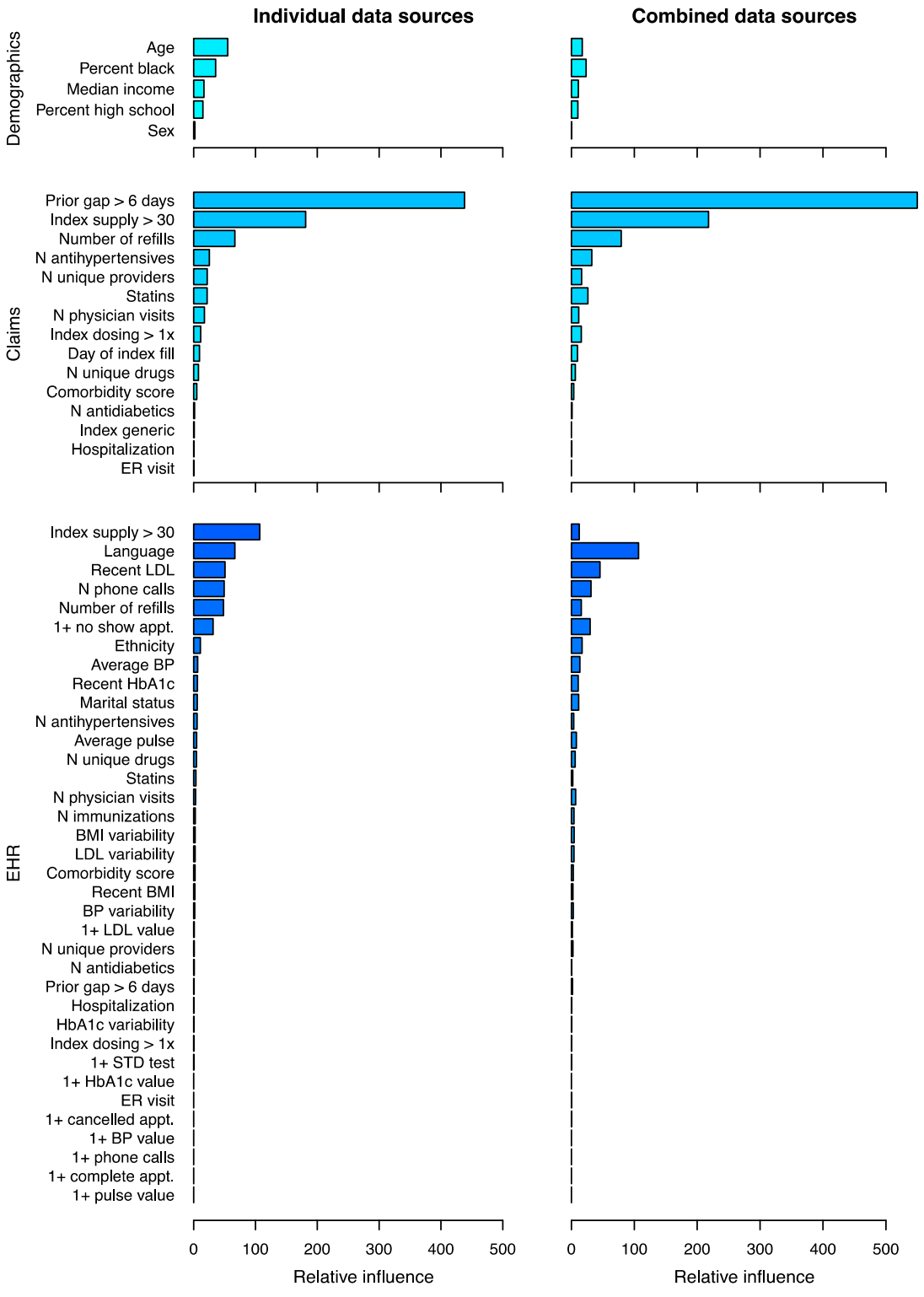
If the goal is instead to identify patients who need immediate intervention, then we seek rules for predicting Trajectory 5 with high NPV to ensure that few patients who truly need intervention are missed. Using either claims or EHR data, the NPV typically decreases with more restriction, while the number of patients assigned to Trajectory 5 requiring intervention also decreases. Assuming that no more than 15% of patients can be intervened upon, the best NPVs result from the models (94% and 93% for claims and EHR, respectively).

Discussion

The ability to predict nonadherence is of increasing importance to many sectors of the health care industry, including providers who increasingly have financial incentive to improve long-term medication use. While claims are widely used to predict nonadherence, providers often do not have access to them or can access them only at substantial delay. In our analysis, we found that a relatively small set of variables derived from claims can provide very good prediction, particularly for identifying patients who are likely to have very poor or very good adherence. However, when claims were not available, EHR data alone could provide predictions with moderate to good accuracy. When both data sources were used, accuracy was highest, although it was not significantly better than claims alone.

When interpreting our results, it is important to note that the accuracy of the predictions from claims in this study was generally higher than that observed in previous studies. Among studies predicting adherence among new medication initiators using baseline data only, C-statistics have been low (<0.65).[22,34-36] When predicting adherence in prevalent users using prior refill adherence, better C-statistics have been reported (0.79),[37] in line

Figure 3



Influence of each variable in predicting trajectory groups.

Table III. Example rules for prediction of the best and worst adherence trajectories using claims data alone or EHR data alone

	Trajectory 1 (Best)				Trajectory 5 (Worst)			
Prediction rules	Value	% of patients	PPV	NPV	Value	% of patients	PPV	NPV
No information		100.0%	57.0%	–		100.0%	9.3%	–
Claims data								
Prior gap	≤6 days	26.8%	77.1%	50.4%	>6 days	73.2%	11.7%	97.1%
+ N refills	≥4	3.7%	80.4%	43.9%	< 4	65.7%	11.8%	95.4%
+ Index supply	>30	1.3%	82.0%	43.4%	≤30	17.1%	28.7%	94.7%
Model top 10%		10.0%	81.7%	45.8%		10.0%	34.4%	93.5%
EHR data								
Index supply	>30	68.2%	60.4%	50.3%	≤30	31.8%	17.4%	94.5%
+ Language	English	62.5%	60.9%	49.5%	Non-English	3.5%	16.3%	90.9%
+ LDL	≤130	57.6%	61.6%	49.4%	>130	0.3%	23.8%	90.7%
+ N phone calls	≤10	32.7%	63.8%	47.5%	>10	0.1%	28.0%	90.7%
+ N refills	≤10	32.6%	63.9%	47.5%	>10	0.0%	14.3%	90.7%
+ No show appt.	0	25.9%	65.7%	47.1%	≥1	0.0%	0.0%	90.7%
Model top 10%		10.0%	70.4%	44.5%		10.0%	28.0%	92.8%

For each individual predictor, the value used to assign patients to each trajectory is given. A "+" before the predictor indicates it is combined with the rule above. For all potential rules, the percent of patients assigned to the trajectory based on the rule, as well as the positive predictive value and negative predictive value are given.

with that observed here. The high accuracy of our models may also be partly attributed to the fact that we are focused on predicting trajectory. Membership in the high-adherence trajectory required more consistent filling than what would be required by a typical 80% adherence threshold; therefore, this group may be more homogeneous than the high-adherence group that is typically the focus of prediction. The prediction accuracy in this study is also improved by the use of data on the number of available refills, which is highly related to adherence but has not previously been used in prediction.

The accuracy of predictions from EHR data alone was also better than typically observed, even in other studies using claims. This accuracy may similarly result from the use of trajectories to group patients for prediction, but it may also rely partly on the additional patient data that is available in the EHR but not in claims, such as information on phone calls, laboratory values, and missed appointments. Length of index supply, measured in both claims and EHR, remained highly predictive in EHR data, likely due to high correlation between the claims and EHR versions of the variable. Other variables that were highly predictive in claims were not replicated well from the EHR, including prior gaps in medication coverage and available refills.

The conclusions from our study are limited by the database in which it was conducted. Our study population consisted of a relatively homogeneous group of Medicare Advantage patients with a single health plan, receiving care from a single medical practice in Eastern Massachusetts. Patients in our study were overall highly adherent, possibly because they all had prescription drug coverage through their Medicare Advantage plan. Populations with greater barriers to adherence may be less predictable. In addition, the Medicare Advantage Stars rating system was already in place during the majority of our study period. Some of the quality metrics for this rating system specifically focused on monitoring adherence to the 3 medication classes studied in this paper among Medicare Advantage beneficiaries, which may have also contributed to the high adherence levels observed and would potentially reduce generalizability to other medications.[14]

While the narrow study population was necessary in order to have complete claims and EHR for all patients, it does limit the generalizability of findings. Specifically, other health plans may have different data available on their patients or different levels of misclassification, which would modify the predictive accuracy of the available data. Similarly, the availability and quality of data in EHR is highly dependent on the specific provider. Integrated care providers, such as HVMA, which provided data for this study, are more likely to have relatively complete data on patients for whom they provide care, as any visits across the network feeds to a single EHR system, capturing nearly all outpatient care. In contrast, individual physician practices will typically only have EHR data covering visits with that practice; any care provided by other practices will not be captured. Quality of the EHR database may also vary based on how regularly it is used to record patient data and how functional it is in recording, storing, and organizing data. We also focus on patients who have filled each medication of interest at least once. Patients who never initiate the medication are not included.

Within the claims and EHR data that were available for our study cohort, we used only a small subset of available

information in constructing predictors. Claims additionally contain large quantities of data on the frequency and type of healthcare service utilization, as well as specific diagnoses and procedures. However, previous investigations of this information have not found it to be useful in predicting medication adherence.[34] EHR data also contain detailed information on each healthcare encounter; prediction models that better utilize these data could improve accuracy over our models. Other data mining methods could also improve predictions; however, the approach used in this paper, boosted logistic regression, has been shown to provide good accuracy in a variety of domains.[38]

This study is further limited by its use of pharmacy claims data to measure adherence. Pharmacy claims may misclassify the adherence of patients who fill prescriptions but do not actually take them, which is particularly problematic in the case of fills with longer days' supply. For example, the majority of patients in all 3 cohorts received an index supply of 90 days, so that they were fully covered during each of the first 3 months, regardless of whether they took the medication. However, patients who fail to complete the first fill would be unlikely to return for a refill. Therefore, misclassification of adherence likely diminishes as follow-up continues. Misclassification may also affect measurement of predictors that attempt to capture adherence at baseline, but prior adherence was nonetheless highly predictive in this study.

Conclusion

Based on the results of this study, we conclude that EHR data may be useful for identifying patients that may benefit from adherence interventions, but it is unlikely to improve predictions available from claims alone. Particularly when using prior adherence information for patients who have previously been on the medication of interest, claims alone can provide highly accurate predictions of the most extreme trajectories, patients likely to remain on therapy over the next 12 months and patients likely to struggle with adherence in the near term. However, predictions based on the EHR may still be more useful than claims for targeting patients for adherence improvement interventions if there is a substantial delay in the availability of claims, since many patients may become nonadherent while waiting for adjudicated claims. Future work should further investigate whether information on past medication orders recorded in the EHR can approximate prior filling patterns to improve prediction from EHR data and the targeting of adherence interventions.

Acknowledgements

We are grateful to Angela Tong and Leilani Hernandez for their assistance with programming and data management.

Funding Sources

This work was funded by Merck & Co. The research contract granted Brigham and Women's Hospital right to publication of results as well as final wording of the manuscript.

Disclosures

CM is an employee of Merck. NM was an employee of Merck during the conduct of the research and is now an employee of Boehringer Ingelheim. JK is an employee of Harvard Vanguard Medical Associates.

Appendix. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahj.2017.09.019.

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