Predicting Adherence Trajectory Using Initial Patterns of Medication Filling

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ABSTRACT

Objectives: To evaluate the ability of initial medication dispensings to predict long-term patterns of adherence.

Study Design: A retrospective cohort study of statin initiators enrolled in a Medicare Part D drug plan from CVS Caremark from 2005 to 2008.

Methods: We used group-based trajectory models to classify patients into 6 adherence trajectories based on patterns of statin filling over the year following therapy initiation. Baseline clinical characteristics and indicators of statin filling during the first 2 to 4 months following initiation were used to predict adherence trajectory in logistic regression models, separately within strata of the days' supply of the initial statin dispensing. Cross-validation was used to measure predictive accuracy of models in data not used for model estimation.

Results: Among 77,703 statin initiators, prediction using baseline variables only was poor (cross-validated C statistic ≤0.61). When using 3 months of initial adherence to predict trajectory, prediction was greatly improved among patients with an index supply ≤30 days (0.62 ≤C ≤0.91). With 4 months of initial adherence in the model, prediction was strong for all patients (C ≥0.72), especially for the best and worst trajectories (C = 0.90 and 0.94, respectively, in patients with an index supply ≤30 days; and C = 0.83 and 0.90, respectively, in patients with an index supply >30 days).

Conclusions: Initial filling behavior strongly predicted future adherence trajectory. Predicting adherence trajectories may facilitate better targeting of interventions to patients most likely to benefit.

Am J Manag Care. 2015;21(9):e000-e000

Adherence to maintenance medications for chronic disease remains low, with nearly 50% of patients becoming nonadherent within a year of treatment initiation.[1-3] Poor adherence has far-reaching consequences, including higher rates of adverse events, worse long-term outcomes, and higher healthcare costs.[4,5] Prediction of future nonadherence allows for the design of adherence interventions targeted to individuals who stand to benefit the most, thereby increasing intervention effectiveness and efficiency. Most attempts to predict medication adherence have focused on predicting a binary measure, which categorizes patients as adherent or nonadherent based on a threshold.[6,7] This classification collapses a broad spectrum of potential adherence behaviors into a simple dichotomy and may result in missing important distinctions among unique patient behaviors that can provide information on which patients will respond to an intervention and when.

Group-based trajectory modeling has offered an alternative approach in which individuals are grouped according to their prescription-filling patterns over time. This method has been successfully used in research on health-related behaviors[8-10]; more recently, it has been applied to medication adherence, where trajectories have been shown to summarize longitudinal adherence better than more conventional approaches.[11] By more appropriately categorizing complex nonadherence behaviors, the trajectory approach may aid in the timing and targeting of interventions for those patients likely to benefit.[12]

Whereas the benefits of the trajectory methodology have been demonstrated in describing adherence retrospectively, the ability to predict trajectory group membership a priori has been little studied. Recent research has shown that observing medication-filling behavior in the first 3 months after initiation provides better discrimination between individuals who are and are not adherent versus investigator-specified clinical variables or variables chosen through advanced selection and modeling techniques.[13] Based on

these findings, we sought to evaluate whether initial observations of medication-filling behavior can perform better than investigator-specified clinical characteristics in the prediction of membership into individual adherence trajectories or groupings of several trajectories.

Take-Away Points

Predicting patients' future adherence behavior is important for improving adherence to clinically recommended medications. We have shown that:

- A simple approach that uses only a few variables assessed from pharmacy claims shortly after statin initiation can provide dramatic improvements in prediction over clinical and demographic characteristics.
- When predicting adherence among patients with short initial dispensings, 2-3 months of observation is sufficient; when predicting among patients with 90-day dispensings, 4 months of observation is needed.
- Predicting adherence trajectories, rather than simple dichotomies of adherent or not, may better facilitate targeting of interventions to patients most likely to benefit.

METHODS

Cohort

We used a previously published cohort of Medicare beneficiaries 65 years and older with prescription drug coverage through CVS Caremark who initiated a statin or statin combination drug between January 1, 2006, and December 31, 2008.[13] Diagnostic, healthcare utilization, and demographic data from Medicare Parts A and B and enrollment files were linked to Caremark prescription drug claims. Patients were required to have continuous enrollment in both Medicare and Caremark for 180 days before and 360 days after initiation. Patients were excluded if they experienced a hospitalization lasting greater than 14 days, entered hospice or a nursing home, or died during follow-up. To ensure active benefit use, patients must have had at least 1 drug dispensing and 1 healthcare claim in the 6 months prior to initiation.

We identified clinically relevant cohort characteristics using medical and pharmacy claims incurred during the 180 days before the index date.[2,7,14,15] Demographic information included age, sex, and race. Clinical characteristics included Charlson comorbidity score and type of statin initiated, health services usage, and comorbidities likely to influence adherence to a cardiovascular medication. Health services usage was measured with 5 variables: 1) the total number of unique cardiovascular diagnoses, 2) the number of inpatient hospital admissions, 3) the total length (in days) of all inpatient stays, 4) the number of outpatient physician visits, and 5) the distinct number of drugs (assessed at the generic drug level). The presence of specific conditions was assessed using *International Statistical Classification of Diseases Ninth Revision (ICD-9)* codes and included acute coronary syndrome (with and without revascularization), prior or recent coronary artery bypass grafting, angina, atrial fibrillation, chest pain, congestive heart failure, hypertension, ischemic heart disease, prior or recent myocardial infarction, peripheral vascular disease, postsurgical aortocoronary bypass, stroke, transient ischemic attack, chronic obstructive pulmonary disease, Alzheimer's disease, depression, cancer, diabetes, kidney disease, and end-stage renal disease.

The Brigham and Women's Hospital Institutional Review Board approved this study.

Adherence Measure

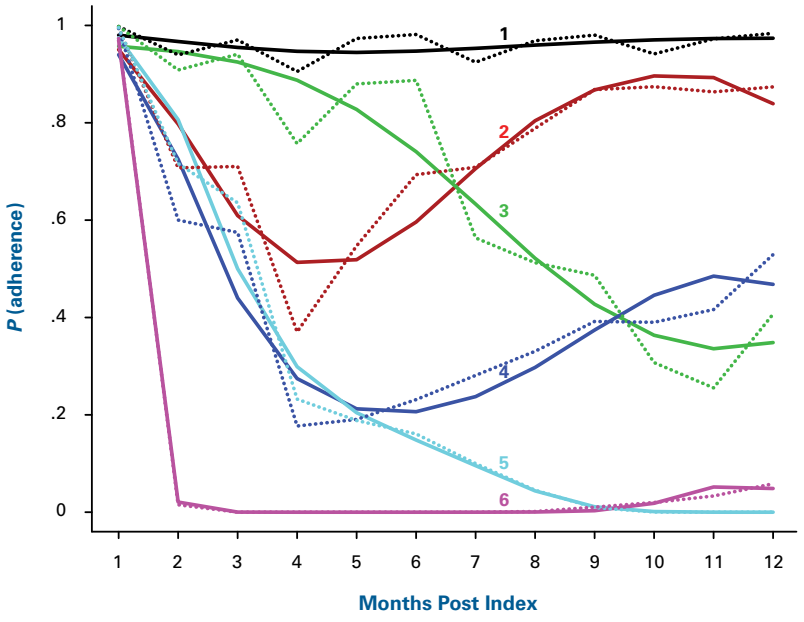
We created a "supply diary" for each patient in the cohort, indicating whether medication was available on each day during the 360 days of follow-up. This diary linked all observed statin fills based on the dispensing date and the days' supply. We calculated the proportion of days covered (PDC) during each of 12 consecutive 30-day periods of follow-up and created a binary indicator for "full adherence" each month, defined as PDC ≥0.8 (or ≥24 days covered, equivalently). This PDC value corresponds to the level of use above which patients with coronary artery disease benefit from statins[16] and the threshold employed by most quality measures.[17,18]

We then modeled these 12 binary indicators as a longitudinal response in a logistic group-based trajectory model. In a trajectory model, several regression models are estimated simultaneously, including a multinomial logistic model that estimates the probability of membership in each group, and ordinary logistic models, which estimate the probability of being adherent over time as a smooth function of time. We estimated our model using 6 adherence groups, which have been observed in prior research to provide the best overall model fit.[11] In each group, we used a third-order polynomial (linear, squared, and cubic terms) of time to model the probability of being adherent. On the basis of these models, we assigned patients to a trajectory group. We implemented this model with "PROC TRAJ," a free downloadable add-on package to base SAS version 9.3 (SAS Institute, Cary, North Carolina). This estimation procedure has been shown to be superior for identifying underlying longitudinal trajectories.[19]

Adherence Prediction

We used the binary indicators of full adherence during the 2 to 4 months immediately following statin initiation and baseline patient clinical and demographic charac-

Figure 1. Observed and Predicted Probability of Adherence During Each Month of Follow-up for Each of 6 Groups Identified by the Trajectory Model



Observed is indicated with dotted lines and predicted is indicated with solid lines.

teristics to predict each patient's observed 12-month adherence trajectory. To predict membership in a given trajectory, we estimated a multivariable logistic regression model with the trajectory group of interest compared with all others as the outcome. All models were run separately based on the length of the patient's index statin fill (ie, ≤30 and >30 days' supply); prior research has demonstrated important differences in the discriminative ability of predictive models based on this stratification factor.[13]

For each trajectory group, we first estimated a model that included only demographic and clinical characteristics. We then estimated 3 additional models that included the clinical predictors as well as the indicators of observed adherence during the first 2, 3, and 4 months after initiation and all interactions as predictors of a future adherence pattern. We repeated these models with different binary groupings of trajectories as the outcome to see if model discrimination improved when trajectory groups with similar behavior were combined.

Prediction models were evaluated with respect to their ability to discriminate between patients assigned to different trajectory groups. Discrimination is measured by the C statistic, a measure ranging from 0.5 to 1.0, corresponding to a completely noninformative model and perfect prediction, respectively.[20] Although the indicators of adherence during the months following initiation contribute to the adherence trajectory that is being predicted, they do not completely determine trajectory grouping[21]; therefore, these models measure the extent to which long-term adherence can be predicted based on initial adherence. We performed 10-fold cross-validation to avoid the "over optimism" bias associated with evaluating model prediction accuracy in the same data that were used to estimate the model.[22]

RESULTS

Cohort Characteristics

Among more than 1 million patients who filled at least 1 prescription for a statin during the study period, 215,542 met the inclusion criteria of continuous enrollment, health services use, and no statin use during the 180 days prior to the index statin prescription. An additional 1687 patients were excluded due to age, and 136,062 had less than 360 days of follow-up, leaving a cohort of 77,703 statin initiators—45,251 of whom had an initial prescription length of 30 days or less. The average age was 74.5 years, and 59% of the cohort was female. The prevalence of full statin adherence each month for patients in each trajectory group is shown in Figure 1. Mean age, index statin type, and prevalence of individual comorbidities were similar across trajectories (Table). Compared with the highest performing trajectory (trajectory group 1), patients in the worst-performing trajectory (trajectory group 6) had more cardiovascular diagnoses (mean = 4.2 vs 3.5), took more distinct drugs (mean = 8.4 vs 7.7), and had higher Charlson comorbidity scores (mean =1.4 vs 1.3).

Adherence Prediction

Among patients with an initial statin fill of 30 days or less, C statistics from multivariable logistic regression models using only baseline clinical predictors resulted in the greatest discrimination when predicting membership in trajectory group 1 versus groups 2 through 6, or when predicting membership in groupings of trajectories such as groups 1 through 3 versus all other groups (Figure 2). However, even in the best models, prediction accuracy was relatively weak (C ≤0.61). When observations of statin adherence during the first 2 months of follow-up were added to the

Table. Patient Characteristics of Statin Initiators in Medicare Receiving Prescription Drug Coverage From CVS Caremark, 2006 to 2008 (separately by adherence trajectory group)

	Trajectory Group					
	1	2	3	4	5	6
Characteristics	**N = 25,313**	**N = 9943**	**N = 10,687**	**N = 12,209**	**N = 11,095**	**N = 8456**
Age, years (mean)	74.34	74.41	74.67	74.48	74.24	74.68
Female sex	61.57	58.72	62.60	61.11	57.80	56.62
Race						
White	56.79	64.58	52.86	60.54	64.42	68.42
Black	12.30	7.78	10.14	7.50	7.06	4.92
Other/unknown	30.91	27.64	37.00	31.96	28.51	26.67
Index statin						
Atorvastatin calcium	40.36	42.24	33.73	38.61	43.17	39.50
Ezetimibe/simvastatin	11.95	11.51	11.97	11.54	11.50	10.30
Fluvastatin sodium	1.26	1.20	1.19	1.42	1.30	1.15
Lovastatin	5.47	4.74	6.48	5.27	4.85	5.35
Pravastatin sodium	6.40	7.17	7.73	7.31	7.06	7.89
Rosuvastatin calcium	11.01	10.79	12.14	12.28	11.35	9.93
Simvastatin	23.55	22.34	26.78	23.56	20.76	25.88
Health services (mean)						
Cardiovascular diagnoses	3.51	3.83	3.95	3.74	3.58	4.24
Hospitalizations	0.18	0.21	0.26	0.21	0.18	0.25
Total hospital length of stay	1.02	1.26	1.55	1.20	1.07	1.60
Physician visits	4.07	4.32	4.18	4.20	4.20	4.28
Distinct drugs	7.74	8.11	7.91	7.93	7.90	8.41
Comorbidity						
Charlson comorbidity score (mean)	1.29	1.35	1.40	1.30	1.26	1.41
Acute coronary syndrome	7.76	8.67	9.56	9.12	8.80	10.53

(continued)

models, discrimination greatly improved, particularly for models predicting membership in trajectory groups 1 or 6 (C = 0.79 and 0.84, respectively). C statistics reached above 0.9, representing very high prediction discrimination, when predicting membership in trajectory 6 using baseline characteristics plus 3 months of initial adherence data. Similar high discrimination was observed when predicting membership in trajectory 1 or in the grouping of trajectories 1 through 3 using baseline characteristics plus 4 months of initial adherence data. Membership in trajectories 2 through 5 could be predicted with moderate discrimination (C = 0.72, 0.77, 0.75, and 0.75, respectively).

Among patients with an initial statin fill greater than 30 days, prediction accuracy when using only baseline clinical predictors was strongest when predicting trajectory group 6, but even this had only modest discriminative ability (C = 0.67). Prediction of this group was near perfect when adding in any initial adherence variables. All other trajectories or trajectory groupings were predicted poorly when using baseline clinical characteristics and up to 3 months of initial adherence indicators (C ≤0.59). However, when using 4 months of initial adherence indicators, discrimination was greatly improved for all adherence groupings, ranging from 0.65 for prediction of trajectory 3 versus all others, up to 0.84 for prediction of trajectories 1 through 3 versus 4 through 6.

DISCUSSION

In this cohort of Medicare beneficiaries initiating treatment with statins, we found that initial adherence during the first few months after initiation strongly predicted the 12-month adherence trajectory. Prediction was best when predicting consistent medication use (trajectory 1)

Table. Patient Characteristics of Statin Initiators in Medicare Receiving Prescription Drug Coverage From CVS Caremark, 2006 to 2008 (separately by adherence trajectory group) *(continued)*

	Trajectory Group					
	1	2	3	4	5	6
Acute coronary syndrome/revascularization	2.57	3.55	3.59	3.68	3.34	5.26
Prior CABG	3.78	4.51	3.76	3.84	3.84	4.66
Recent CABG	0.61	1.06	0.84	1.07	0.90	1.59
Angina	6.76	7.33	7.83	7.63	7.32	8.23
Atrial fibrillation	1.63	1.98	2.53	2.27	1.89	2.84
Chest pain	18.70	17.59	20.98	19.31	17.30	18.75
Congestive heart failure	8.78	9.42	10.16	9.08	8.54	10.79
Hypertension	71.04	71.50	72.56	71.79	70.14	73.80
Ischemic heart disease	7.79	9.10	9.25	8.65	7.87	10.36
Recent MI	1.44	2.32	2.48	2.23	1.86	3.61
Prior MI	3.11	3.43	3.56	3.29	3.16	3.90
Peripheral vascular disease	1.32	1.67	1.67	1.71	1.57	2.03
Postsurgical aortocoronary bypass	3.63	4.41	3.68	3.77	3.74	4.50
Stroke	1.40	2.01	2.78	2.12	1.83	2.73
Transient ischemic attack	2.68	3.18	3.65	3.34	2.75	3.44
COPD	3.50	3.46	4.15	3.62	3.71	3.36
Alzheimer's disease	3.29	3.56	3.62	3.19	3.08	4.24
Depression	3.52	4.32	3.68	3.93	3.91	4.29
Cancer	15.18	17.25	15.46	16.15	17.65	17.81
Diabetes	36.62	36.21	35.32	34.26	35.38	35.44
Kidney disease	4.39	5.26	5.15	4.90	4.15	5.65
ESRD	0.81	0.76	1.02	0.71	0.59	0.62

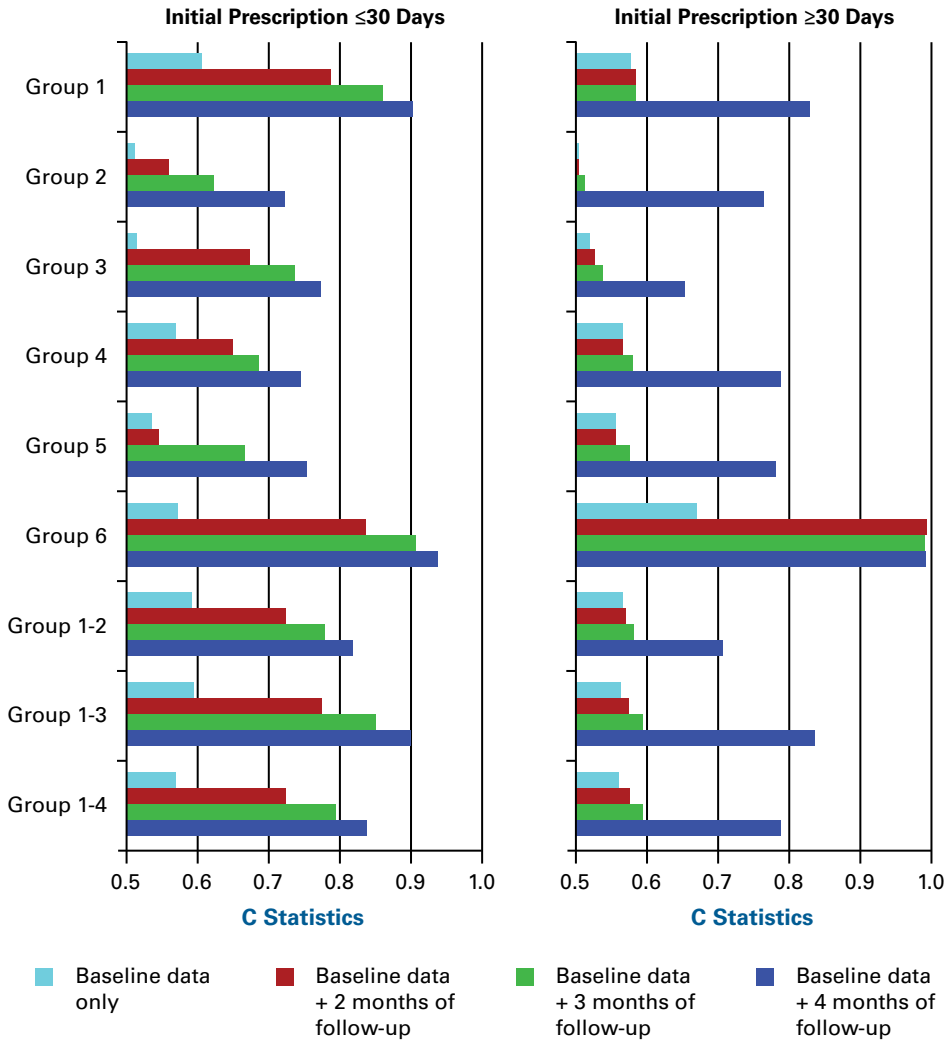
CABG indicates coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; MI, myocardial infarction. Because the study size is large, all patient characteristics are significantly associated with the trajectory group using analysis of variance (ANOVA) for continuous variables and χ^2 tests for categorical variables.
All values are % unless otherwise indicated.

and consistent nonuse (trajectory 6) or when predicting the combination of groups 1 through 3 versus 4 through 6. Among patients with an index prescription longer than 30 days, accurate predictions for most trajectories required observing adherence for 4 months after initiation—likely because this window provides an opportunity to observe the presence or absence of a refill among patients with a 90-day index prescription. In all cases, prediction using initial adherence observations was much stronger than prediction from baseline clinical characteristics alone.

These results confirm and extend results previously reported in studies of adherence. Identified adherence trajectories were very similar to those observed in other cohorts of statin initiators.[11] Poor prediction of adherence from baseline characteristics alone has also been observed across a range of medications, especially in the study of statins.[6,7,11,23,24] The high accuracy of adherence predictions based on initial filling behavior is similar to that recently observed when predicting whether patients will be optimally adherent over the 12-month period following initiation based on a PDC threshold of ≥0.8.[13] However, accuracy when predicting the most extreme trajectories (1 and 6) was even stronger than accuracy in predicting optimal adherence. In addition, prior research did not evaluate the effect of including a fourth month of adherence observations to the predictions, which appears to be crucial for patients with 90-day index fills.

Predicting adherence trajectory rather than PDC may be useful for focusing interventions on patients with moderate medication use—for example, patients falling in trajectories 2 through 5. These patients are not perfect adherers, but they also have not completely discontinued

Figure 2. Cross-Validated C Statistics for Predicting Adherence Trajectory Groups



The vertical axis indicates which group or groups are the focus of prediction (compared with all other groups). For example, results for "groups 1-2" quantify discrimination from a model predicting membership in groups 1 or 2 versus groups 3 through 6. Prediction was based on baseline clinical characteristics alone or augmented with 2, 3, or 4 months of initial adherence indicators.

their medication. Therefore, patients with these dynamic patterns may be most susceptible to potential interventions that encourage adherence and those that help moderate adherers refill more regularly or avert discontinuation.

In addition, interventions may be especially effective if deployed at specific times (eg, just prior to or in the early stages of nonadherence). Unlike PDC, trajectory groupings differentiate between patients who struggle with adherence at different times during their medication use. For instance, patients in group 4 were identified well after observing 4 months of initial adherence. For these patients, this time coincides with a steep decline in adherence, followed by a period of sporadic medication use. Targeted interventions for patients predicted to be in group 4 could be implemented at this time, and these interventions may be systematically different in structure and timing than those targeted to patients predicted to be in group 6. Filling behavior from the first 3 or 4 months would therefore be highly actionable, even in the presence of administrative delays in the receipt of claims data.

Limitations

Our study was restricted to patients who demonstrated active use of the healthcare system and who remained en-

rolled in both Medicare and their Part D drug plan for 180 days before and 365 days after their initial statin dispensing. This group may not be representative of all statin initiators in Medicare though, since the patients in our study maintained stable drug coverage for at least 18 months. Prediction performance observed in our study may also not hold in a younger working population receiving statins or when predicting adherence to other chronic disease medications.

As in prior studies of medication adherence, our study is also limited by the accuracy of assessing adherence from pharmacy claims data, which may misclassify the adherence of patients who fill prescriptions but do not actually take them. However, we expect this issue to be of less practical importance in patients with short, frequent dispensings. The potential for misclassification is also diminished as the period of adherence follow-up is lengthened, since patients who do not take their medications generally do not continue to fill those medications. The use of pharmacy claims additionally prevents us from evaluating the reason for nonadherence, including clinically appropriate discontinuation due to side effects; however, based on prior research, we expect this number to be low.[2]

CONCLUSIONS

In this study, 12-month trajectories of statin use were well predicted by observations of adherence during the first 2 to 4 months after initiation, but could not be predicted accurately by clinical characteristics measured at baseline. Therefore, physicians, pharmacy benefit managers, or other providers with timely access to patient refill data could easily implement a dynamic prediction system for adherence trajectories. The trajectories observed in this study were similar to those observed previously, but individual providers may wish to optimize their prediction system by re-estimating the trajectory models in their specific patient population and with a specific number of groups corresponding to different adherence interventions. Because both the trajectory model and the prediction model methodology are relatively simple and require little beyond pharmacy refill data, highly accurate predictions are possible for a wide spectrum of patients at providers with varying resources.

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Source of Funding: This work was supported by an unrestricted grant from CVS Caremark to Brigham and Women's Hospital.

Author Disclosures: Drs Shrank, Brennan, and Matlin are employees of CVS Health, which builds and supplies proprietary algorithms predicting medication adherence; Drs Brennan and Matlin are also CVS stockholders. The remaining authors report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Authorship Information: Concept and design (JMF, WHS, TAB, NKC); acquisition of data (NKC, TAB); analysis and interpretation of data (JMF, AAK, OSM, NKC); drafting of the manuscript (JMF, AAK); critical revision of the manuscript for important intellectual content (JMF, AAK, WHS, OSM, TAB, NKC); statistical analysis (JMF, AAK); obtaining funding (OSM); administrative, technical, or logistic support (OSM); and supervision (WHS).

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REFERENCES

1. Avorn, J, Monette J, Lacour A, et al. Persistence of use of lipid-lowering medications: a cross-national study. *JAMA*. 1998;279(18):1458-1462.

2. Benner JS, Glynn RJ, Mogun H, Neumann PJ, Weinstein MC, Avorn J. Long-term persistence in use of statin therapy in elderly patients. *JAMA*. 2002;288(4):455-461.

3. Choudhry NK, Setoguchi S, Levin R, Winkelmayer WC, Shrank WH. Trends in adherence to secondary prevention medications in elderly post-myocardial infarction patients. *Pharmacoepidemiol Drug Saf*. 2008;17(12):1189-1196.

4. DiMatteo MR, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. *Med Care*. 2002;40(9):794-811.

5. Roebuck MC, Liberman JN, Gemmill-Toyama M, Brennan TA. Medication adherence leads to lower health care use and costs despite increased drug spending. *Health Aff (Millwood)*. 2011;30(1):91-99.

6. Raebel MA, Ellis JL, Carroll NM, et al. Characteristics of patients with primary non-adherence to medications for hypertension, diabetes, and lipid disorders. *J Gen Intern Med*. 2012;27(1):57-64.

7. Chan DC, Shrank WH, Cutler D, et al. Patient, physician, and payment predictors of statin adherence. *Med Care*. 2010;48(3):196-202.

8. Caldeira KM, O'Grady KE, Garnier-Dykstra LM, Vincent KB, Pickworth WB, Arria AM. Cigarette smoking among college students: longitudinal trajectories and health outcomes. *Nicotine Tob Res*. 2012;14(7):777-785.

9. Conklin CA, Perkins KA, Sheidow AJ, Jones BL, Levine MD, Marcus MD. The return to smoking: 1-year relapse trajectories among female smokers. *Nicotine Tob Res*. 2005;7(4):533-540.

10. Hong SI, Hasche L, Bowland S. Structural relationships between social activities and longitudinal trajectories of depression among older adults. *Gerontologist*. 2009;49(1):1-11.

11. Franklin JM, Shrank WH, Pakes J, et al. Group-based trajectory models: a new approach to classifying and predicting long-term medication adherence. *Med Care*. 2013;51(9):789-796.

12. Cutrona, SL, Choudhry NK, Fischer MA, et al. Targeting cardiovascular medication adherence interventions. *J Am Pharm Assoc (2003)*. 2012;52(3):381-397.

13. Franklin JM, Shrank WH, Lii J, et al. Observing versus predicting: initial patterns of filling predict long-term adherence more accurately than high-dimensional modeling techniques. *Health Serv Res*. 2015. doi:10.1111/1475-6773.12310.

14. Mann DM, Woodward M, Muntner P, Falzon L, Kronish I. Predictors of nonadherence to statins: a systematic review and meta-analysis. *Ann Pharmacother*. 2010;44(9):1410-1421.

15. Kulik A, Shrank WH, Levin R, Choudhry NK. Adherence to statin therapy in elderly patients after hospitalization for coronary revascularization. *Am J Cardiol*. 2011;107(10):1409-1414.

16. Choudhry NK, Glynn RJ, Avorn J, et al. Untangling the relationship between medication adherence and post-myocardial infarction outcomes: medication adherence and clinical outcomes. *Am Heart J*. 2014;167(1):51-58.e5.

17. Medicare health & drug plan quality and performance ratings: 2013 Part C & Part D technical notes. CMS website. https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovGenIn/Downloads/Technical-Notes-2013-.pdf. Published 2013. Accessed October 15, 2014.

18. HEDIS measures. National Committee for Quality Assurance website. http://www.ncqa.org/Portals/0/HEDISQM/HEDIS2014/List_of_HEDIS_2014_Measures.pdf. Published 2014. Accessed October 15, 2014.

19. Twisk J, Hoekstra T. Classifying developmental trajectories over time should be done with great caution: a comparison between methods. *J Clin Epidemiol*. 2012;65(10):1078-1087.

20. Harrell FE Jr, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med*. 1996;15(4):361-87.

21. Jones BL, Nagin DS. Advances in group-based trajectory modeling and an SAS procedure for estimating them. *Sociol Methods Res*. 2007;35(4):542-571.

22. Steyerberg EW, Harrell FE Jr, Borsboom GJ, Eijkemans MJ, Vergouwe Y, Habbema JD. Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. *J Clin Epidemiol*. 2001;54(8):774-781.

23. Steiner JF. Can we identify clinical predictors of medication adherence... and should we? *Med Care*. 2010;48(3):193-195.

24. Steiner JF, Ho PM, Beaty BL, et al. Sociodemographic and clinical characteristics are not clinically useful predictors of refill adherence in patients with hypertension. *Circ Cardiovasc Qual Outcomes*. 2009;2(5):451-457. ■

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