Original research

Patterns and predictors of physician adoption of new cardiovascular drugs

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ABSTRACT

Background: Little is known about physicians' approaches to adopting new cardiovascular drugs and how adoption varies between drugs of differing novelty.

Methods: Using data on dispensed prescriptions from IMS Health's Xponent™ database, we created a cohort of all primary care physicians (PCPs) and cardiologists in Pennsylvania who regularly prescribed anticoagulants, antihypertensives and statins from 2007 to 2011. We examined prescribing of three new cardiovascular drugs of differing novelty: dabigatran, aliskiren and pitavastatin. Outcomes were rapid adoption of each new drug, defined by early and sustained monthly prescribing detected by group-based trajectory models, by physicians within the first 15 months of marketplace introduction.

Results: 5953 physicians regularly prescribed each drug class. The majority of physicians (63.8%) adopted zero new drugs in the first 15 months, 35.0% rapidly adopted one or two, and 1.2% rapidly adopted all three. Physicians were more likely to rapidly adopt the most novel drug, dabigatran (27.3%), than aliskiren (10.5%) or pitavastatin (8.0%). Physician specialty and sex were the most consistent predictors of adoption. Compared to PCPs, cardiologists were more likely to rapidly adopt dabigatran (Adjusted Odds Ratio 8.90, 95% confidence interval 7.42–10.67; P < 0.001) aliskerin (2.05, CI 1.56–2.69; P < 0.001) and pitavastatin (3.44, CI 2.60–4.57; P < 0.001). Female physicians were less likely to adopt dabigatran (0.71, CI 0.59–0.85; P < 0.001) and aliskiren (0.64, CI 0.49–0.83; P < 0.001).

Conclusions: Physicians vary in their prescribing of recently-introduced cardiovascular drugs. Though most physicians did not rapidly adopt any new cardiovascular drugs, drug novelty and cardiology training were associated with greater adoption.

Over the past decade the US Food and Drug Administration has approved over 300 new drugs, giving physicians a broad array of new medications of varying therapeutic novelty to treat and prevent disease.[1] Innovative therapies targeting cardiovascular diseases have substantially reduced global morbidity and mortality.[2] Yet diffusion of new cardiovascular drugs has been uneven, characterized both by

underuse of evidence-based, cost-effective therapies[3–6] and by overuse of some high-cost medications with minimal therapeutic advantage over existing therapies.[7]

Escalating prices have driven prescription drug spending into the spotlight of health policy debates. Policymakers initially focused on controlling patient demand for new drugs by encouraging the use of

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generic drugs through tiered formularies.[8] More recent proposals have targeted industry pricing practices[9,10] and emphasized value-based initiatives designed to help physicians and patients better understand the risks, benefits and costs of new therapies.[11,12]

Whether and how new drug introductions lead to changes in patient care or expenditures ultimately depends on the speed and frequency with which physicians adopt them.[13] To achieve more optimal diffusion, whereby physicians adopt truly innovative medicines and seldom prescribe those with little marginal benefit will likely require targeted interventions. Yet, little is known about how physicians approach prescribing of new drugs. Prior studies show that the speed with which US physicians adopt new drugs is correlated with specialty, practice setting, age, sex, and training.[14–19] However, whether a given physician brings a consistent propensity to adopt all drugs or differentiates adoption based on a drug's novelty is poorly understood because prior studies of physician adoption focus on a single drug or class.

We examined adoption of three newly-introduced drugs that nevertheless varied in the extent to which they represented a therapeutic advance over existing products. We examined adoption in the first 15 months post marketplace introduction: dabigatran, a first-in-class oral anticoagulant; aliskiren, a first-in-class antihypertensive; and pitavastatin, the seventh statin, to answer three questions designed to inform future value-based prescribing interventions. First, does physician adoption vary with drug novelty? Second, do individual physicians take a consistent approach to adopting all drugs? Third, what are the characteristics of physicians who rapidly adopt new drugs across multiple classes?

1. Methods

1.1. Data sources

We obtained monthly physician-level data on prescriptions dispensed for anticoagulants, antihypertensives and statins from IMS Health's Xponent™ database, which captures over 70% of all US prescriptions filled in retail pharmacies and uses a patented proprietary projection methodology to represent 100% of prescriptions filled in these outlets. Xponent™ includes data on the number of filled prescriptions for the drug classes of interest regardless of payer for patients of all ages. Prescribing data was linked to data on physician characteristics from the American Medical Association (AMA) Masterfile, which includes demographics, specialty and medical education for all US physicians. Physicians' organizational affiliations were determined using IMS Health's Healthcare Organizational Services (HCOS) Database, which captures over 29,000 practices, clinics, hospitals and integrated health systems.

1.2. Study population

We examined monthly prescribing data for all physicians practicing in Pennsylvania who regularly prescribed anticoagulants, antihypertensives and statins. We then limited the sample to physicians with a record in the AMA Masterfile and HCOS databases (Fig. 1). As physician specialty was a major variable of interest and primary care physicians (PCPs) and cardiologists made up over 90% of prescribers of these medications, we limited our sample to those two specialty groups. To measure adoption among actively practicing physicians we required ≥1 prescription fill in each drug class in each quarter of the year before new drug introduction and each year after new drug introduction.

1.3. Study drugs

Our analytic approach examines the influence of drug novelty on adoption of three drugs in three classes of cardiovascular drugs. As such, we are unable to distinguish between novelty and class effects on physician adoption behavior. The ideal experiment to clarify the
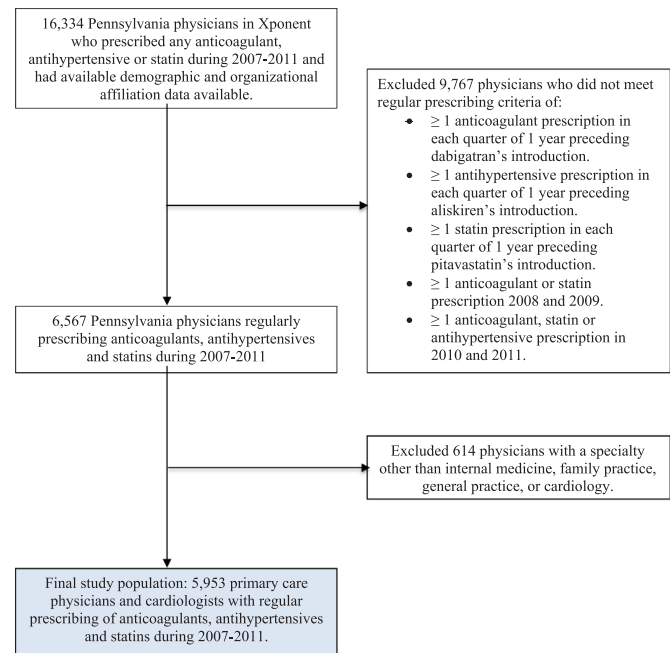

Fig. 1. Prescriber study population flow chart.

influence of novelty on physician adoption would examine the introduction of multiple drugs of the varying novelty within the same class, at the same time. However, this experiment is not feasible, as drugs of differing novelty within the same class are rarely introduced in the same timeframe. Comparing adoption across extended time periods risks confounding due to external time-sensitive policies and changes in the study-base of physicians. We focused on cardiovascular drugs as they are widely prescribed by both primary care physicians and cardiologists, and in each drug class there are multiple therapeutic options with largely similar efficacy across patient populations. We examined the prescribing of three recently approved cardiovascular drugs of differing novelty for which alternatives existed prior to the study drug introduction.

Drug novelty was determined using previously accepted definitions which incorporate novel drug mechanism, therapeutic advantage, safety and convenience.[20,21] The most novel study drug, dabigatran was the first new oral anticoagulant approved for treatment of atrial fibrillation. Dabigatran represents the first addition to the anticoagulant market since warfarin and an important advance given similar efficacy in stroke prevention, modest reductions in major bleeding compared to warfarin and no requirement for regular blood monitoring.[22] A second, moderately novel drug, was aliskiren, the first direct renin inhibitor approved for treatment of hypertension. Direct renin inhibitors are the third class of antihypertensives to target the renin-angiotensin system, and studies demonstrate efficacy and tolerability profiles similar to other classes[23,24] but they have not been endorsed as first-line treatments.[25] At the time of aliskiren introduction, there were 40 alternative antihypertensive medication formulations. We considered pitavastatin, the seventh statin to be introduced in the US, to be the least novel of the study drugs as it has the same mechanism of action as existing drugs and clinical trials show it has similar efficacy compared to existing statins.[26]

We examined study drugs that were introduced in a relatively narrow timeframe (2007–2010). Given data availability, we imposed the same follow up period for all drugs. Prescribing of each drug was studied from month of FDA approval to 15 months following introduction: March 2007 to May 2008 for aliskiren, June 2010 to August 2011 for pitavastatin, and October 2010 to December 2011 for dabigatran.

1.4. Measuring adoption

Studies of physician adoption of new drugs typically measure adoption using the time to first prescription of the new drug.[14–17] However, this measure does not capture heterogeneity in uptake of a drug once it is first prescribed. For example, time to first prescription may misclassify a physician as a rapid adopter if she writes a single prescription for a drug even if she is refilling a prescription initiated by another physician. To provide a more complete measure of adoption, we examined patterns of prescribing using group-based trajectory models, which identify individual prescribing changes over time and characterize subgroups more likely to follow certain adoption trajectories.[27,28] We defined adopters as those with early and sustained monthly prescribing of each drug.

1.5. Covariates

We included a number of physician covariates including demographics (sex, years since medical school graduation), training characteristics (graduation from a US medical school, graduation from a top-20 medical school,[29] and specialty) and prescribing characteristics (average monthly prescribing volume for each drug class). We also included variables related to the physician practice including: patient-payer mix (percentage of physician's prescriptions paid for by Medicare, fee-for-service Medicaid, commercial insurance, and cash), share of prescriptions written for various age groups, metropolitan vs. non-metropolitan practice location, and practice size.

1.6. Statistical analysis

To overcome the limitation of traditional linear regression in uncovering distinct adoption behavior over time, we fit group-based trajectory models for the number of monthly prescriptions separately for each drug to identify differential patterns of prescribing. Group-based trajectory modeling is an application of finite mixture modeling that classifies a heterogeneous distribution of population longitudinal trajectory into several homogeneous trajectory subgroups.[30,31] Within the same group, individuals follow approximately the same trajectory. We transformed the raw numbers of monthly prescriptions using the inverse square root function, and then modeled the transformed numbers of monthly prescriptions as a longitudinal continuous outcome, with months since marketplace introduction was the time variable. The transformed numbers of prescriptions were modeled using a censored normal distribution with no minimum and a maximum of one. We used the most flexible polynomial form of time to allow the trajectories to emerge from the data. For each group, the order of the polynomial function was determined by the Wald test with a significance level of 0.05. The output of group-based trajectory models includes estimated probabilities of group membership for each individual, and an estimated average trajectory curve over time for each group. Plot values were transformed back to the original scale with the inverse square function. Individuals were assigned to the group for which they had the highest estimated probability. The final models were selected based on the Bayesian information criterion (BIC), wherein the largest value indicates the best-fitting model.[27,28] We used the Nagin's criteria to assess final model adequacy. The Nagin's criteria of a well-performed trajectory model include with average posterior probability ≥ 0.7 for all groups, odds correct classification ≥ 5.0 for all groups, estimated probability of membership in each group close to the proportion of sample assigned to each group, and narrow confidence intervals.

1.7. Identifying rapid adopters

We defined rapid adopters as physicians in either of the two highest prescribing trajectory groups, as these two groups exhibited early and sustained drug prescribing compared to the remaining trajectory groups

in all three drug classes. We estimated the number of physicians who rapidly each study drug and for each drug separately, we used a multivariable logistic regression model to identify characteristics associated with rapid adoption using all of the covariates described above. Statistical significance was determined using 95% confidence intervals (CI) and two-tailed tests with $P < 0.05$.

We performed two sensitivity analyses. First, as an alternative to using trajectory groups, we defined rapid adopters as physicians who wrote two or more prescriptions for the drug of interest within the study period. The results were qualitatively similar to our primary analyses so we present only our primary findings. Second, as an alternative to using number of prescriptions as the outcome in the trajectory models, we used average monthly *share* of drug class prescriptions for each study drug. Due to the overall low levels of pitavastatin and aliskiren uptake, analyses using share of prescriptions classified too few physicians as rapid adopters to permit multivariable analyses of predictors of adoption. All analyses were conducted in SAS version 9.3 (SAS Institute Inc., Cary, NC).

2. Results

2.1. Descriptive characteristics of study sample

A total of 5953 physicians regularly prescribing the three classes of interest were included in the study sample. During the study period, physicians wrote a total of 1,390,088 prescriptions for anticoagulants, 8,149,594 prescriptions for anti-hypertensives, and 9,406,605 prescriptions for statins. Of these, 68,506 (4.9%) of anticoagulants prescriptions were for dabigatran, 26,104 (0.3%) anti-hypertensive prescriptions were for aliskiren and 12,144 (0.1%) statin prescriptions were for pitavastatin.

Table 1 shows the characteristics of the study physicians who were predominately male (75.2%), trained in US medical schools (81.1%) and had over 20 years of practice since medical school (67.7%). Most were PCPs (83.8%) and the remainder were cardiologists. Baseline prescribing volume varied by drug class; physicians prescribed a larger mean number of antihypertensives (103.7 per month) and statins (91.7 per month) than anticoagulants (16.5 per month). Compared to PCPs, cardiologists wrote a greater monthly mean number of anticoagulants (22.6 versus 15.1) and a smaller monthly mean number of anti-hypertensives (70.2 versus 110.1) and statins (70.4 versus 95.9). Study physicians' prescriptions were reimbursed by a diverse set of payers, with a similar mix for each class.

2.2. Trajectories of prescribing

Fig. 2 depicts the results of group-based trajectory modeling. For each drug, models using five distinct prescribing groups provided the best fit (Supplemental Table 1). Fig. 2A depicts the five trajectory groups for dabigatran. Although 54.5% (n = 3243) wrote ≥ 1 prescription for dabigatran, only 27.3% (n = 1628) were classified as rapid adopters with early and sustained prescribing. One group of rapid adopters (A) prescribed a monthly average of three dabigatran prescriptions starting 6 months post-market introduction and continued that level of prescribing throughout the study period with a small drop off at month 15 when rivaroxaban (competitor of dabigatran) entered the market. Another group of rapid adopters (B) demonstrated sustained prescribing, though slightly later, averaging over one prescription/month by month 9. Of the remaining physicians, 15.2% (C) had minimal prescribing until 12 months, 12.2% (D) had minimal prescribing throughout, and 45.2% (E) wrote zero dabigatran prescriptions during the study period.

Trajectory groups demonstrated similar patterns for aliskiren (Fig. 2B), though it was less widely ever prescribed (n = 1451 or 24.4%) and rapid adopters of aliskiren accounted for a smaller percentage of physicians (n = 624 or 10.5%) with one group of rapid adopters (A)

Table 1

Descriptive characteristics of physicians prescribing anticoagulants, antihypertensives and statins before and after new drug introductions.

Sources: Xponent™ database 2007–2011, HCOS™, IMS Health Incorporated. All Rights Reserved.

Characteristic	Physicians		
Physicians, N	5953		
Sex, N (%)			
Female	1474 (24.8)		
Male	4479 (75.2)		
Medical school, N (%)			
US medical school graduate	4826 (81.1)		
Top 20 US medical school	579 (9.7)		
Specialty, N (%)			
Cardiology	966 (16.2)		
Primary care	4987 (83.8)		
Years since medical school graduation, N (%)			
< 10	309 (5.2)		
10–19	1617 (27.2)		
20–29	2142 (36.0)		
30 +	1885 (31.7)		
Location of practice, N (%)			
Metropolitan	5263 (88.4%)		
Non-metropolitan	690 (11.6%)		
Practice size, N (%)			
No medical group affiliation	670 (11.3%)		
Small medical group (1–5 providers)	2451 (41.2%)		
Medium medical group (6–40 providers)	2298 (38.6%)		
Large medical group (41 + providers)	534 (9.0%)		
Mean monthly prescribing volume (SD)	**Statins**	**Anticoagulants**	**Antihypertensives**
All physicians	91.7 ± 64.2	16.3 ± 15.5	103.7 ± 75.3
Cardiologists	70.4 ± 56.4	22.6 ± 20.5	70.2 ± 58.4
Primary care physicians	95.9 ± 64.8	15.1 ± 14.0	110.1 ± 76.5
Mean patient-payer mix for prescriptions (SD)			
Cash + Medicaid fee-for-service	7.5% ± 9.0%	9.3% ± 12.5%	9.3% ± 9.5%
Commercial insurance*	57.6% ± 16.6%	48.7% ± 19.9%	60.6% ± 15.8%
Medicare	34.9% ± 13.4%	42.0% ± 18.3%	30.1% ± 12.6%
Mean patient age mix for prescriptions (SD)			
00–64 years	50.2% ± 15.0%	33.3% ± 20.7%	50.6% ± 20.7%
65–84 years	42.2% ± 11.9%	51.3% ± 18.8%	40.3% ± 12.4%
85+ years	7.5% ± 6.5%	15.4% ± 13.3%	9.1% ± 6.8%

Note: Analyses use IMS Health's Xponent™ and HCOS™ linked with American Medical Association Masterfile data.

* Commercial insurance includes Medicaid managed care.

prescribing a monthly average of 3 prescriptions by month 6 and another group (B) prescribing a monthly average of 1 prescription by month 8. The pitavastatin trajectory groups demonstrated similar features as described for aliskiren (Fig. 2C), though even fewer ever prescribed (n = 1065 or 17.9%) or rapidly adopted pitavastatin (n = 474 or 8.0%). The rapid pitavastatin adopter group (A) prescribed an average of just under 2 prescriptions/month by month 7 while group (B) had regular prescribing of an average of over one prescription/month by month 9.

2.3. Discrimination in adoption across classes

Nearly two-thirds (63.8%) of physicians appeared to take a conservative approach to all three adoption decisions and did not adopt any new drugs (Fig. 3). Of the remaining physicians, 1658 (27.9%) selectively, rapidly adopted a single drug, the majority dabigatran, and 423 (7.1%) selectively adopted two drugs. Only 74 physicians (1.2%) were broad adopters of all three new drugs.

2.4. Predictors of adoption

Specialty practice was the strongest predictor of rapid adoption (Table 2). Cardiologists were much more likely to rapidly adopt each drug compared with PCPs after adjusting for other covariates (OR 8.90, 95% CI [7.42–10.67] for dabigatran; 2.05 [1.56–2.69] for aliskiren; 3.44 [2.60–4.57] for pitavastatin; all $P < 0.001$). Female physicians were significantly less likely to adopt dabigatran (OR 0.71 [0.59–0.85], $P < 0.001$) and aliskiren (OR 0.64 [0.49–0.83], $P < 0.001$) than male

physicians. Graduates of top-20 ranked medical schools were more likely to adopt dabigatran (OR 1.35 [1.08–1.69], P = 0.008) and less likely to adopt aliskiren (OR 0.53 [0.36–0.77], P < 0.001) or pitavastatin (OR 0.65 [0.42–0.97], P = 0.03).

3. Discussion

Our study finds that physicians were generally conservative in adopting new cardiovascular drugs, with a minority of physicians adopting dabigatran, aliskiren or pitavastatin in the first 15 months of marketplace introduction. Among study physicians rapidly adopting any new drugs, far more took a selective approach than an indiscriminate approach with only 3.4% rapidly adopting all three drugs. Physician specialty was the strongest predictor of new drug adoption, with cardiologists being much more likely to adopt all three new drugs compared to PCPs.
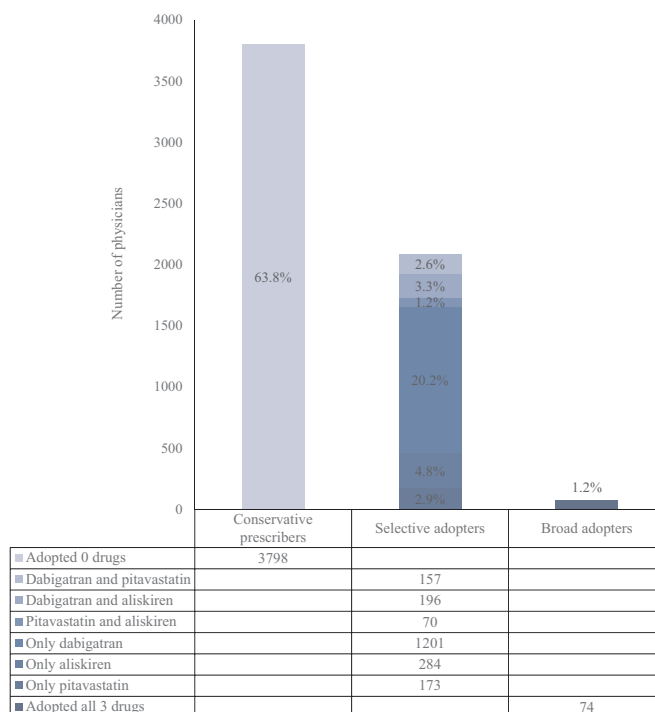
Physicians have incomplete information on the relative safety and effectiveness of new drugs. Initial clinical trials are often too small to detect rare side effects and manufacturers typically do not have to demonstrate comparative effectiveness to gain regulatory approval.[32] Some experts have cautioned physicians to be 'conservative' prescribers, waiting to adopt new drugs until post-marketing information is available.[33] However, when a new drug offers a significant improvement in efficacy or safety, delaying prescribing may be more risky.[34] Ideally, physicians will prescribe the safest, most cost-effective medication for a given health condition, balancing the known risks, benefits, and costs with uncertainty over yet to be determined harms.

Efforts to improve value-based prescribing may emphasize the rapid

A) Dabigatran

B) Aliskiren
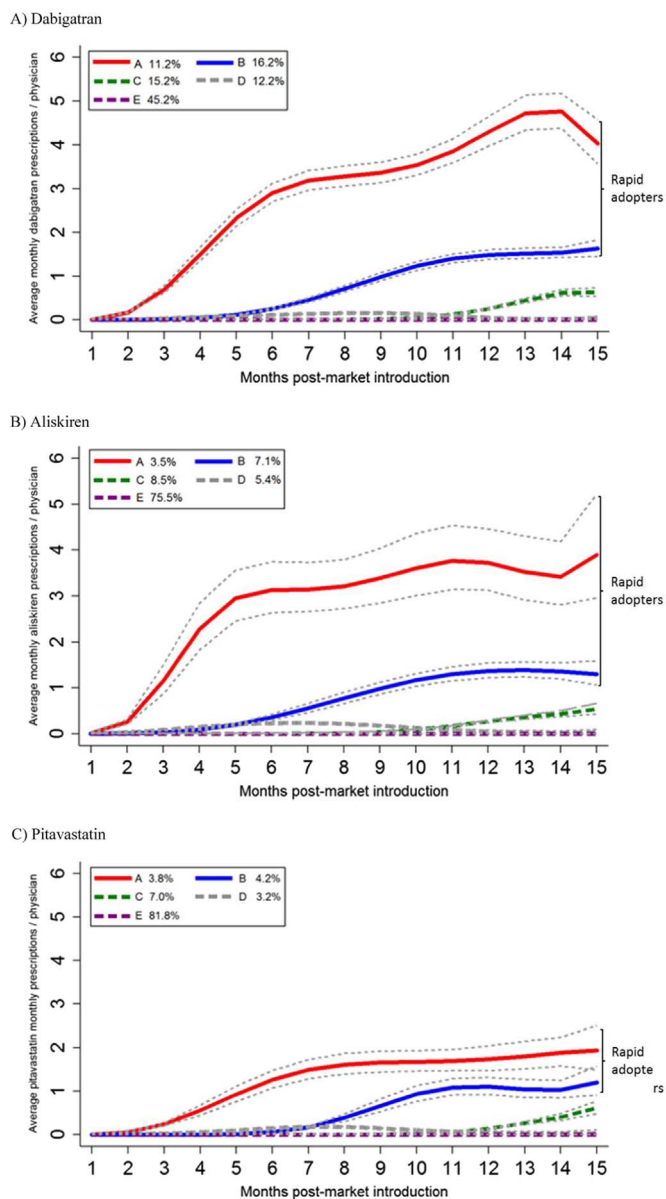
C) Pitavastatin

Fig. 2. A-C: Trajectory grouping of adoption of cardiovascular medications [*]. A) Dabigatran. B) Aliskiren. C) Pitavastatin [*] The predicted probability of adoption of each drug in each group is plotted with thick solid or dashed lines. The thin dotted lines are 95% confidence intervals for the predicated probabilities.
Source: Xponent™ database 2007–2011, IMS Health Incorporated. All Rights Reserved.

	Conservative prescribers	Selective adopters	Broad adopters
▢ Adopted 0 drugs	3798		
▢ Dabigatran and pitavastatin		157	
▢ Dabigatran and aliskiren		196	
▢ Pitavastatin and aliskiren		70	
▢ Only dabigatran		1201	
▢ Only aliskiren		284	
▢ Only pitavastatin		173	
▢ Adopted all 3 drugs			74

Fig. 3. Physician adoption of dabigatran, aliskiren and pitavastatin by in first 15 months of market introduction.* * Physician adoption of each drug was defined by trajectory group modeling of prescribing in first 15 months of marketplace introduction, individuals classified in the top two highest prescribing groups were classified as adopters. Conservative prescribers were defined as those who adopted zero new drugs, selective adopters as those who adopted one or two new drugs, and broad adopters as those who adopted all three new drugs.
Source: Xponent™ database 2007–2011, IMS Health Incorporated. All Rights Reserved.

adoption of truly novel drugs or the reduction of indiscriminate adoption of all new products.[11,33,34] Our finding that physician adoption appeared to differ by drug novelty expands on prior studies by looking across drug classes. Although future studies will need to expand the number of drug classes studied to disentangle the effects of novelty from medication class, our findings may have implications for future educational interventions. Physician adoption patterns tended to follow evidence on comparative effectiveness, as the most novel drug studied, dabigatran, a first-in-class oral anticoagulant with modest reductions in major bleeding compared to warfarin[12] was the most widely adopted. Fewer physicians adopted aliskiren, a first-in-class medication but one that lacks improvements in efficacy or safety over existing antihypertensives.[13,14] Finally, pitavastatin, the seventh statin was adopted by the fewest number of physicians. For health systems and payers, it may be cost-effective to identify the relatively small group of physicians who broadly adopted all three new drugs to better target value-based educational interventions such as academic detailing.

Targeting interventions towards individual prescribers may be labor intensive, thus identifying key characteristics of rapid adopters can help policymakers target interventions at a population level. In this study, cardiologists were significantly more likely to adopt each of the three drugs compared with PCPs, after controlling for prescribing volume. While cardiologists may see a greater number of eligible patients with atrial fibrillation thus driving a higher propensity to prescribe dabigatran, they were also significantly more likely to prescribe pitavastatin and aliskiren even though they accounted for a lower share of prescribing volume in the antihypertensive and statin classes than did PCPs. Cardiologists may see a greater proportion of high-risk cardiovascular patients and may be more willing to prescribe new agents for hypertension and hyperlipidemia if older drugs have failed; however, to our knowledge neither aliskiren nor pitavastatin have been studied in higher risk patients. Cardiologists prescribe a more narrow set of drugs compared with PCPs and thus may be better positioned to rapidly digest evidence on new drugs or they may have been more heavily targeted by pharmaceutical sales representatives promoting these particular products.[35,36]

Medical schools may influence adoption through their policies governing contact with pharmaceutical representatives and by transmitting norms and information from educators to students.[37,38] The finding that physicians who graduated from top ranked medical schools were more likely to adopt dabigatran and less likely to adopt pitavastatin or aliskiren suggests that training institution may influence prescribing behavior. Future studies aimed at identifying what components of medical training influence adoption may be important for guiding interventions to address evidence-based prescribing after licensure.

A physician's propensity to adopt is driven not only by features of the drug but also by characteristics of physicians themselves.[39,40] Prior studies of single drug classes have suggested prescribing of new

Table 2

Physician characteristics associated with odds of adoption of dabigatran, aliskiren and pitavastatin.
Sources: Xponent[TM] database 2007–2011, HCOS[TM], IMS Health Incorporated. All Rights Reserved.

Characteristics[*]	Dabigatran adopters[a]		Aliskiren adopters[a]		Pitavastatin adopters[a]	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Sex						
Male	Reference		Reference		Reference	
Female	0.71 (0.59, 0.85)	< 0.001	0.64 (0.49, 0.83)	< 0.001	0.79 (0.60, 1.05)	0.11
Medical school location						
US	Reference		Reference		Reference	
Foreign	1.06 (0.89, 1.26)	0.55	1.03 (0.81, 1.30)	0.81	1.36 (1.05, 1.77)	0.02
Medical school ranking						
Other	Reference		Reference		Reference	
Top 20	1.35 (1.08, 1.69)	0.008	0.53 (0.36, 0.77)	< 0.001	0.65 (0.43, 0.97)	0.03
Specialty						
Primary care	Reference		Reference		Reference	
Cardiology	8.90 (7.42, 10.67)	< 0.001	2.05 (1.56, 2.69)	< 0.001	3.44 (2.60, 4.57)	< 0.001
Years of practice						
< 10	Reference		Reference		Reference	
10–19	0.79 (0.56, 1.13)	0.19	1.32 (0.68, 2.58)	0.42	0.90 (0.53, 1.55)	0.71
20–29	0.77 (0.55, 1.09)	0.14	1.19 (0.61, 2.33)	0.61	0.57 (0.33, 0.98)	0.04
30 +	0.65 (0.46, 0.93)	0.02	1.17 (0.60, 2.31)	0.64	0.59 (0.34, 1.03)	0.06
Location of practice						
Metropolitan	Reference		Reference		Reference	
Non-metropolitan	1.13 (0.92, 1.39)	0.23	0.95 (0.72, 1.24)	0.68	1.06 (0.78, 1.45)	0.70
Practice size						
Individual practice	Reference		Reference		Reference	
Small group (1–5 providers)	1.73 (1.35, 2.23)	< 0.001	1.50 (1.01, 2.16)	0.03	1.94 (1.26, 3.00)	0.003
Medium group (6–40 providers)	1.42 (1.11, 1.82)	0.006	1.21 (0.83, 1.75)	0.32	1.34 (0.86, 2.08)	0.19
Large group (41 + providers)	1.96 (1.44, 2.67)	< 0.001	0.81 (0.50, 1.32)	0.39	0.54 (0.29, 1.00)	0.051
Average monthly prescribing volume for each drug class	Anticoagulants		Antihypertensives		Statins	
	1.05 (1.05, 1.06)	< 0.001	1.01 (1.01, 1.013)	< 0.001	1.01 (1.011, 1.014)	< 0.001
Patient-payer mix for each drug class						
Commercial	Reference		Reference		Reference	
Medicaid or cash	0.14 (0.06, 0.31)	< 0.001	0.24 (0.06, 0.96)	0.04	0.03 (0.004, 0.17)	< 0.001
Medicare	0.56 (0.36, 0.86)	0.009	2.15 (0.71, 6.48)	0.18	0.67 (0.21, 2.12)	0.50
Patient age mix for each drug class						
0–64	Reference		Reference		Reference	
65–84	2.59 (1.63, 4.12)	< 0.001	0.32 (0.10, 1.06)	0.06	0.21 (0.05, 0.81)	0.02
85 +	2.25 (1.24, 4.09)	0.008	1.18 (0.21, 6.80)	0.85	0.23 (0.02, 2.66)	0.24

Note: Analyses use IMS Health's Xponent[TM] and HCOS[TM] linked with American Medical Association Masterfile data.
  * Table shows the results of three logistic regression models estimating the odds of adopting each of the three drugs.
  [a] Physician adoption of each drug was defined by trajectory group modeling of prescribing in first 15 months of marketplace introduction; individuals classified in the top two highest prescribing groups were classified as adopters.

medications may be influenced by physician sex.[14–19] Consistent with prior studies, we find that for two of our three drugs male physicians were more rapid adopters than female physicians.[39] These differences may arise from differences in patient case-mix between female and male physicians[41] although we did adjust for the patient age distribution of physician and payer mix.

Our study has several notable strengths and limitations. The major strength was the use of all-payer data on three widely prescribed drug classes; however; findings for these classes may not be generalizable to other drug categories with different types of competition. Second, our analytic approach examines the influence of novelty on adoption of drugs in three different classes, as such, we are unable to distinguish

between novelty and class effects on physician adoption behavior. The ideal experiment to clarify the influence of novelty on physician adoption would examine the introduction of multiple drugs of the varying novelty within the same class. This ideal experiment is not feasible, as drugs of differing novelty within the same class are rarely introduced in the same timeframe. Examining prescribing of different drugs over an extended period of time is likely to result in confounding due to external time-sensitive policies and changes in the study-base of physicians. For example, lovastatin, the first drug in the statin class was approved in 1987 while pitavastatin was approved in 2009. In this two-decade timeframe, many physicians have started practice or retired, influential clinical trials on statin efficacy have been published,

guidelines and indications for statin use have changed and policies pertaining to prescription drug benefits have been enacted. Thus comparing the introduction of lovastatin in 1987 to pitavastatin in 2009 would be to compare different physician populations at times when there were markedly different indications for prescribing. As the ideal experimental approach is not feasible, our study is designed to compare drugs of differing novelty within related and widely prescribed cardiovascular classes which were introduced over a narrow timeframe.

Third, we used group-based trajectory modeling to improve upon earlier measures of adoption based on time to first prescription, an approach which may misclassify one-time prescribers as adopters of a drug. Our results demonstrate that, nearly half of physicians who prescribed each new drug at least once did not go on to regularly prescribe the drug (54.5% vs 27.3% for dabigatran, 24.4% vs 10.5% for aliskiren and 17.9% vs 8.0% for pitavastatin). We found similar results in a sensitivity analysis defining adoption as two or more prescriptions during the study period. Third, our study examined all prescribers in Pennsylvania, which as the 6th most populous state with socioeconomic and health care utilization demographics close to national averages offers a strong approximation for the entire country. Nonetheless, our findings may not generalize to other states. We lacked information on the diagnosis associated with prescriptions so we cannot adjust for difference in patient mix across physicians. To account for the impact of training on physician prescribing, we included a covariate for graduation from a top-20 medical school, however due to limited availability of rankings data we could only estimate the rankings in 2013 and not at time of medical school enrollment. We were not able to measure all potential confounders, most notably data on physician receipt of drug detailing or direct to consumer advertising was not available for our study period. Finally, our data included only prescriptions dispensed, thus our results may be confounded by factors affecting patients' decisions to fill prescriptions.

4. Conclusion

We find that the majority of physicians are conservative in adopting new cardiovascular drugs within the first 15 months of introduction. Physicians who did rapidly adopt tended to selectively adopt dabigatran, a novel anticoagulant. These findings suggest that initiatives to improve the value of physician prescribing will require targeting initiatives, which may include both promotion of high-value new therapies and deterrence of adoption of low-value therapies, towards specific physician populations and drug classes.

Conflict of interest disclosures

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. The authors report no conflicts of interest related to this manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.hjdsi.2017.09.004.

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