ORIGINAL RESEARCH

Pharmacoeconomics 2006; 24 Suppl. 3: 65–78
1170-7690/06/0003-0065/$39.95/0

Impact of Medicaid Preferred Drug Lists on Therapeutic Adherence

David B. Ridley[1] and *Kirsten J. Axelsen*[2]

1 Duke University, The Fuqua School of Business, Durham, North Carolina, USA
2 Pfizer Inc., New York, New York, USA

Abstract

Objective: To estimate rates of non-adherence for statins following implementation of a preferred drug list (PDL).

Study design: A retrospective cohort study.

Methods: A difference-in-difference-in-difference approach was used to estimate the impact of a PDL on the use of statins in an Alabama Medicaid population. The PDL restricted access to certain branded medications and imposed a monthly prescription limit. The use of restricted drugs was compared with the use of unrestricted drugs in the months before and after the PDL in North Carolina (where there were no such restrictions) and Alabama. Pharmacy data from 2001 to 2005 were used to examine the effect of the Alabama PDL implemented in 2004.

Results: Following the PDL in Alabama, Medicaid beneficiaries treated with statins had an 82% higher relative odds of becoming non-adherent with statin therapy compared with North Carolina and with pre-PDL Alabama [odds ratio (OR) 1.82, 95% CI 1.57, 2.11]. Furthermore, patients taking a restricted statin were more likely to be non-adherent than unrestricted patients (OR 1.42, 95% CI 1.12, 1.80). In addition, among Medicaid beneficiaries taking a restricted statin, people aged 65 years or older were more likely to be non-adherent than their younger counterparts after the PDL (OR 1.33, 95% CI 1.02, 1.73). Fifty-one per cent of patients in the Alabama sample were non-adherent with statin therapy after the PDL, compared with 39% before. Non-adherence was 36% in North Carolina in both periods.

Conclusion: The management of heart disease and high cholesterol are important challenges, especially for low-income patients. Policy makers should be aware that access restrictions can have adverse consequences for patient adherence.

Introduction

Government and private insurers impose financial or administrative hurdles that limit patient and physician access to some higher-cost drugs. Such hurdles encourage patients to switch to lower-cost therapeutic substitutes. Furthermore, the threat of such hurdles gives insurers leverage in extracting rebates from pharmaceutical manufacturers.[1] For example, some states use preferred drug lists (PDLs) to encourage Medicaid patients to switch to a therapeutic substitute that is a lower cost for the

insurer. Such policies could lower drug costs while maintaining total utilisation in the drug class. Alternatively, if patients are confused by the prescription change, they might discontinue use, which would decrease utilisation in the class. Such decreased utilisation could harm patient health and increase overall medical costs. We investigate the effect of a PDL on the utilisation of cholesterol-lowering statins by Medicaid patients.

A common cost–control mechanism used by private insurers is a tiered co-payment formulary. In 2005, 74% of workers with employer-sponsored coverage had a cost-sharing arrangement with three or four co-payment tiers.[2] For example, an insurer might charge a patient a $US10 co-payment for a generic drug, a $US20 co-payment for a preferred brand-name drug, and $US35 for a non-preferred brand-name drug. Higher co-payments not only shift costs to patients, but also decrease demand.[3–8] Furthermore, co-payment increases have an even greater effect on demand if a rival in the therapeutic class remains at a lower co-payment level (e.g. $US20 for one name-brand drug and $US35 for its rival).[9]

State Medicaid programmes have not used such three-tier formularies because they are only allowed to charge a nominal co-payment for drugs. Furthermore, they cannot deny a beneficiary a drug based on failure to pay the co-payment.[10] Instead, states require prior authorisation for drugs that are not on the PDL. To obtain prior authorisation, prescribing physicians must interact with the insurer's pharmacy bureaucracy to obtain permission to prescribe the non-preferred drug. A PDL controls pharmaceutical costs by encouraging patients and physicians to choose a drug that costs the insurer less. Presumably, the drugs are close substitutes. A 2005 survey of 36 states and the District of Columbia found that 25 of the 37 used PDLs for some drugs.[11] California is threatening to require prior authorisation for Medicaid drugs if the discounts to Medicaid or to middle-income Californians are insufficient.[12]

Generic substitution (substituting the generic for the brand-name medication) requires only the action of the pharmacist at the point of sale unless the physician has specifically prohibited the substitution. Therapeutic substitution (the substitution of a medication of one chemical entity for another) requires a new prescription from the provider in most states.[13]

We examine the impact of the PDL initiated by Alabama in October 2003 (described in detail in the Data section below). We expect that the PDL will lead to lower drug costs than the state would have faced otherwise. The impact of the PDL on health outcomes and total health costs is uncertain. The PDL, like other cost containment measures, could have three possible effects. First, a physician might stop prescribing non-PDL drugs. Second, a physician might challenge the PDL by submitting a prior authorisation request for permission to continue the non-PDL drug. If approved, the patient would continue the same therapy with full Medicaid coverage for the drug. If rejected, the patient would either switch medications or pay the full price out of pocket. Third, if a physician unknowingly writes a prescription for a non-PDL drug then the pharmacist must charge the patient the full price for the drug or get permission from the physician to change the prescription (which could take several hours or days). Patients might discontinue therapy under these circumstances because of the disruption associated with obtaining a new prescription or because of the disruption from taking a new medication. The limits impose another hurdle for the Medicaid patient. If the patient reaches the limit on a medication in a month she must either pay out of pocket or forgo treatment until the next month.

If her physician prescribes the original (non-approved) drug without obtaining prior authorisation and the patient is denied coverage at the pharmacy, she might be discouraged from pursuing the matter. This might be particularly likely in treatments for asymptomatic conditions. If a patient does not feel the short-term impact of high cholesterol, it might be harder for her to appreciate the long-term value of the drug. Furthermore, Medicaid patients are vulnerable to access restrictions because they typically have many

prescriptions,[14] less education, and less access to health information on the Internet. Transportation costs might also discourage them from seeking follow-up visits with their physicians to rectify coverage problems.

The proportion of physicians who accept Medicaid patients has been declining. Physicians cite low compensation and administrative burdens as reasons they do not accept Medicaid patients.[15] The prior authorisation requirements would increase the administrative burden, and physicians might react to the greater administrative burden by reducing their Medicaid patient caseload.

A second risk for patient discontinuation comes from switching medicines. Even if patients successfully negotiate the system and obtain a PDL-preferred medication, their new medication will not necessarily have the same benefit or side-effect profile (even within the statin class). If the patient feels nauseated, as could easily occur for patients with multiple medical conditions, she might wrongly blame her nausea on the new medication and stop taking it. Different packaging, shape and color could also confuse her about the new drug's purpose and usefulness.

Previous research found mixed results from cost controls. Soumerai et al.[16] found that New Hampshire Medicaid's limits on drug payments resulted in more admissions to hospitals and nursing homes and thus greater overall medical cost. Bloom and Jacobs[17] used a pre-post design to study the impact of prior authorisation for cimetidine in the West Virginia Medicaid programme. The use of cimetidine declined 84% (while national use was increasing), whereas hospitalisations for peptic ulcer disease (which cimetidine treats) increased.

On the other hand, Cromwell et al.[18] found that the Florida Medicaid programme that restricted reimbursement for anti-ulcer drugs reduced outpatient drug utilisation without any significant increase in the rate of hospitalisation for peptic-related conditions. Furthermore, Smalley et al.[19] used time-series data to evaluate prior authorisation for non-generic non-steroidal anti-inflammatory drugs in the Tennessee Medicaid programme. Seemingly minor restrictions on drug choice saved an estimated $US12.8 million over 2 years with no identified increases in the use of other drugs, physician visits, or hospital admissions.

Some outcomes are, however, difficult to quantify. For example, Smalley and colleagues[19] were not able to measure the increase in patient pain and inflammation resulting from a 26% decrease in the use of non-steroidal anti-inflammatory drugs. Furthermore, studies that show no short-term effect from cost controls might not be conclusive because of the challenge of measuring long-term health outcomes.

Tamblyn and colleagues[20] examined the effect of increased cost-sharing of pharmaceuticals on poor and elderly patients in Canada. They found that the policy was followed by reductions in the use of essential drugs and a higher rate of serious adverse events and emergency department visits. Wilson and colleagues[21] examined the effect of a PDL on Medicaid patients in a large midwestern state. They found that patients were 39% more likely to discontinue hypertension therapy after the restriction was implemented.

Tamblyn et al.[20] and Wilson et al.[21] identified the effects of policies by comparing variables before and after the policy. We used a similar methodology, but rather than using a single difference (over time) we used three differences (over time, across states, and across drugs). Our study also differs from previous research in that we examined the use of statins in Medicaid populations.

Statins significantly reduce the incidence of coronary heart disease-related morbidity and mortality and strokes in patients undergoing treatment for an average of 5 years.[22–27] Statins are important for national health, because cardiovascular disease has been the number one killer in the United States every year since 1919. Cardiovascular disease kills 2500 Americans each day.[28] We focussed on Alabama where heart disease accounts for 29% of all deaths.[29]

Statins can play an important role in enhancing patient health and life, but patients often fail to

adhere to their prescription regimens.[30,31] Furthermore, insurers often try to decrease spending on statins, because statins are one of the highest drug spending categories. In fact, two statins, atorvastatin and simvastatin, were the top selling drugs in the United States in 2003[32] the year before Alabama implemented its PDL for statins.

Attempts to control statin costs can, however, disrupt medical treatment in vulnerable populations, and have adverse consequences for patient health and long-term costs.

Our analysis examined three questions: (1) Did the restrictions have a measurable effect on a patient's likelihood of discontinuing statin therapy? (2) Did the restriction have a measurable effect on the likelihood that an existing patient's medication would be switched? (3) Did the patients taking a restricted medication have a higher increase in discontinuation than patients taking unrestricted medicines?

Data and Methods

Data

Alabama initiated a PDL in October 2003. The state phased in drugs by therapeutic category. Alabama restricted skeletal muscle relaxants beginning in December 2003; four brand-name statin medications beginning in March 2004 (although generic versions are available without restrictions); and hypertension, hypotension, other non-statin hyperlipidemics, and attention deficit hyperactivity disorder medications beginning in March and April 2004. In addition to the PDL, Alabama imposed a limit of four branded medications and ten total medications per patient per month. In other words, Alabama would not cover a fifth branded medication with a few exceptions (e.g. antiretrovirals, antipsychotics).[33]

We compared Alabama with North Carolina because North Carolina did not have a PDL for statins and because it is a southern state with similar patient demographics. For 2003–4, Medicaid enrollment was 14.8% in Alabama and 14.6% in North Carolina. The median annual income was $US38 111 in Alabama and $US39 000 in North Carolina.[34]

Verispan Inc. provided the prescription data for the study. Medicaid prescription data in Verispan are drawn primarily from retail pharmacy chains, pharmacy software used by independent pharmacies to submit claims, and pharmacy switch processors. The data captured directly from the pharmacies included 100% of all transactions in the pharmacy. The full Verispan dataset includes 50–55% of US retail prescriptions.

The sample included prescriptions filled between December 2001 and February 2005. We selected pharmacies for which Verispan had consistently received data since December 2001, so the sample included 151 pharmacies in Alabama (out of 1165 captured in Verispan data) and 298 in North Carolina (out of 1637).

The prescription data included the name of the drug, quantity supplied, date of fill, days supplied of prescription, the county code of the pharmacy and the age and sex of the patient. Records for the same patient were linked over time using Verispan's HIPAA-compliant unique and anonymous patient identifier.

The Verispan data included patient age and the county code for the pharmacy in which the prescription was filled. The 2000 Census provided county-level data on the percentage of the county that was urban, African-American, white non-Hispanic, and had households with income less than 150% of the federal poverty level. We matched unique individuals to the county of the most frequently used pharmacy then used the county-level data from the Census to infer demographic characteristics for the individual.

Patients were included in the post-PDL group if they had a statin prescription paid by Medicaid in the 3 months before PDL implementation restricting statin medications (December 2003 to February 2004) and they had also filled a statin prescription before December 2003. Patients were selected for the pre-PDL group under the same selection methodology, but shifted one year earlier (with a statin prescription filled between December 2002 and February 2003, in addition to a statin

prescription in 2001). Patients were excluded if they were less than 18 years old.

For both groups, electronic pharmacy records were extracted for all statin prescriptions. We selected prescriptions for the study based on the Medicare United States Pharmacopeia guidelines for 2004.[35]

For individuals in the post-PDL groups in both states, all statin prescriptions were selected from March 2003 to February 2005 (one year of pre-PDL data and one year post, including March 2004). The pharmacy records from the post-PDL period of March 2004 to February 2005 were analysed for adherence and switching. We applied the same methodology to the pre-PDL group, which was selected using the same criteria of having a statin prescription during the earlier period of December 2002 to February 2003 using prescription data from March 2002 to February 2004.

These selection criteria identified 1458 patients in Alabama in the pre-PDL group and 1666 patients in Alabama in the post-PDL group (1018, or 42%, were in both groups). North Carolina had 3945 patients in the pre-PDL group and 5086 patients in the post-PDL group (2876 of whom, or 40%, were in both groups). Correlation of the distribution of patients by county in both the pre-PDL and post-PDL groups was 0.99 in both states (significant < 0.01).

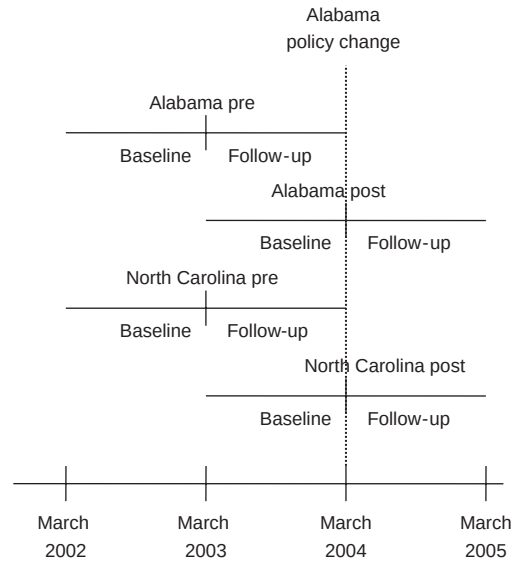

Fig. 1. Illustration of difference-in-difference methodology. We compare statin discontinuation in Alabama after the preferred drug list (PDL) with statin discontinuation in Alabama before the PDL and with statin discontinuation in North Carolina in the period after the Alabama PDL.

Methods

We estimated the impact of the Alabama restrictions using a 'difference-in-difference' model[36,37] with three differences: restricted versus non-restricted drugs, before versus after the PDL, and Alabama versus North Carolina. We controlled for fixed effects so the effect of the PDL in Alabama was identified by the change in Alabama in 2004, relative to North Carolina in 2004 and relative to Alabama in 2003 (figure 1).

We estimate three model specifications. Model A describes the average effect of the PDL on discontinuation in Alabama after the PDL. We normalised with respect to the patient's utility of continuing a drug. The net utility of becoming non-adherent is then given by:

$$U(DISCONTINUE_{it}) = B_1 PDL_{st} + B_2 COUNTY_c + B_3 X_{it} + e_{it}$$

$$U(DISCONTINUE_{it}) = Z_{it}B + e_{it}$$

$$Prob(DISCONTINUE_{it}) = \exp(Z_{it}B)/(1 + \exp(Z_{it}B))$$

where c indexes county, d indexes drugs, i indexes individuals, s indexes states, and t indexes years. In all of the models we assumed that the error term has a logistic distribution that yields the above logit probability. We estimated the logit model using maximum likelihood.

$DISCONTINUE = 1$ if the patient had medication available for fewer than 50% of days in the time period between their first post-PDL refill and the end of the study. (Alternatively, it can be

defined as equalling 1 when the medication possession ratio is less than 50%.) Steiner and Prochazka[38] described this type of dichotomous medication adherence measure and recommended a continuous measurement approach. However, as in Wilson et al.[21] the dichotomous approach was selected for ease of explanation and parameter interpretation. The results are not sensitive to alternative definitions of discontinuation. The magnitude and direction of the findings were similar for all parameters when we estimated a survival model to predict days to discontinuation.

For the post-PDL group, the study period began at the first prescription fill between December 2003 and February 2004 and ended in March 2005. The study period was one year earlier for the pre-PDL group. All statin medications were included in the discontinuation calculation, not just the brand of medication taken at the time the PDL was implemented.

$PDL = 1$ if state s imposed a PDL in year t. *COUNTY* consists of fixed effects for the county of the pharmacy where most prescriptions were filled. This variable is included as a proxy for race or socioeconomic characteristics, which have been shown to affect adherence in other studies and are not available in the Verispan pharmacy claims dataset.[39] Patient sex and the presence of add-on therapy with eztimibe were found to have no significant effect on the non-adherence and were not included in the study.

We included control variables for patient characteristics: age ranges, whether the patient received a statin prescription from a cardiologist, previous days on therapy, and previous non-adherence. *CARDIOLOGIST* equals 1 if a cardiologist prescribed at least 30 days' supply of medication in the observation (post-index) period. *PRIOR-EXPERIENCE* was the number of days supplied of medication in the 12 months before the index period. *PRIOR NON-ADHERENCE* was the number of days supplied of medication in the 12 months before the index period divided by the time between the earliest fill in the 12 months before the index period and the first day of the index period. In other studies, previous time on therapy, previous non-adherence and the use of a specialist affected future adherence.[30,40]

Model B includes the effect of the PDL on a patient taking a restricted drug compared with an unrestricted drug.

$$\begin{aligned} U(DISCONTINUE_{it}) &= B_1 PDL_{st} + B_2 RESTRICTED_d \\ &+ B_3 PDL_{st} * RESTRICTED_d \\ &+ B_4 COUNTY_c + B_5 X_{it} + e_{it} \end{aligned}$$

$RESTRICTED = 1$ if the patient filled a prescription for atorvastatin, pravastatin, or rosuvastatin during the sample period. These three statins were not restricted in 2003 in either state, but were restricted in 2004 in Alabama only. In both 2003 and 2004, $RESTRICTED = 1$ for these drugs, but $PDL = 1$ only in March 2004 or later.

Model C includes an interaction term for senior patients to estimate the incremental effect of the PDL on non-adherence in elderly beneficiaries taking restricted medication.

$$\begin{aligned} U(DISCONTINUE_{it}) &= B_1 PDL_{st} + B_2 RESTRICTED_d \\ &+ B_3 PDL_{st} * RESTRICTED_d + B_4 PDL_{st} \\ &* RESTRICTED_d * AGE65_i \\ &+ B_5 COUNTY_c + B_6 X_{it} + e_{it} \end{aligned}$$

Finally, we examined switching. We classified a patient as switched if she took a different medication in the current month than in the previous month. Changes from branded to generic versions of the same medication were not considered switching. A restricted switch was indicated if the patient changed from a restricted medication to an unrestricted medication during the study period. We present the results of this descriptive analysis but do not explicitly include it in the model because switching is so highly correlated with taking a restricted drug during the post-PDL period (93% of all patients switched were on a restricted drug in the post-PDL period), which is already included explicitly in the model.

Results

Table I presents the demographic characteristics of the counties in which the prescriptions were filled by patients in the sample. We constructed the table by matching the county in which the patient filled the prescription to the county-level demographic characteristics in the 2000 Census. The sample size for Alabama was smaller than for North Carolina because the population of Alabama is approximately half that of North Carolina.[41] The North Carolina counties represented in the sample appear to have similar demographic characteristics to the Alabama counties. In both states the patients in the sample were approximately 69% white. Alabama is slightly more rural and poor. These results are consistent with state-level data from the Kaiser Family Foundation. In 2003–4, 70% of Alabama residents and 66% of North Carolina residents were white. The median annual income was $US38 111 in Alabama and $US39 000 in North Carolina.[42]

Table II and table III present descriptive characteristics of inferred patient demographics and of the medication behaviour of the patients in the sample. The demographics and baseline medicine utilisation of sample populations in both states in both periods are quite similar. In the post-PDL time period, time on therapy and days supply filled is lower in Alabama. Days between prescriptions, percent of patients seeing a cardiologist and patients with MPR <50% is higher in the post-PDL time period in Alabama.

Table IV presents the proportion of patients switching drugs. Before the PDL both Alabama and North Carolina had similar rates of switching (8% and 7%, respectively) and only 3% of switching was from a restricted to a non-restricted drug. After the PDL the Alabama switching rate increased to 50%, with 47% switching from a restricted to a non-restricted drug.

The decision tree in figure 2 illustrates the rates of discontinuation in Alabama according to whether the patient switched, whether the patient was taking a restricted therapy, and whether the PDL was in effect. Sixty-seven per cent of patients began the pre and post-PDL observation period with a prescription for what became a restricted medication in March 2004. In the post-PDL period, 72% of individuals taking a restricted drug switched medications compared with 11% in the pre-PDL period. The group taking restricted medications that switched medications did not have a higher discontinuation rate relative to the pre-PDL group. Of the 28% who took a restricted medication and who did not switch in the post-PDL group, the vast majority (92%) discontinued. The remaining 8% who did not discontinue presumably were approved for prior authorisation or paid out of pocket for their prescription. There was little switching for the non-restricted population. However, the discontinuation rate was also higher for this group (46% post-PDL vs 38% pre-PDL).

Figure 3 illustrates the effect of the PDL in 2004. We plotted the number of prescriptions filled by each patient cohort over time. We normalised prescriptions in each state to 100. Statin prescriptions fell over time for all groups. The most dramatic drop, however, occurred for patients in Alabama after the implementation of the PDL in 2004.

Table I. Characteristics of the counties in which the prescriptions were filled

State	PDL	n	% Urban	% African American	% White	% of households below 150% of federal poverty level
Alabama	Pre-Alabama PDL	1664	56	28	69	28
	Post-Alabama PDL	1771	56	28	68	28
North Carolina	Pre-Alabama PDL	4520	60	24	69	22
	Post-Alabama PDL	5562	61	24	69	22

PDL = preferred drug list, or same equivalent time period in North Carolina.

Table II. Characteristics of the patients in the sample

State	PDL	n	% of Days with no Rx between first and last Rx, baseline period	Days of therapy, baseline period	% on Restricted drug[a]	Follow-up period					
						% of Patients for whom cardiologist prescribed 30+ days' supply	Total time on therapy (in days) in study period	Days between prescriptions	Patients who had medication < 50% of days	% of Days with medication	Days supply of therapy in study period
Alabama	Pre-PDL	1664	16	194	67	9	296	59	39	58	246
	Post-PDL	1771	18	194	67	11	262	63	51	49	205
North Carolina	Pre-PDL	4520	16	197	66	8	301	59	36	60	252
	Post-PDL	5562	16	192	66	8	299	57	36	60	252

[a] At the start of the follow-up period.
PDL = preferred drug list.

Table V presents the results from the logistic model predicting the probability of discontinuation. The main finding is that after the PDL in Alabama, individuals had 82% higher relative odds of discontinuing statin therapy compared with North Carolina and with pre-PDL Alabama (model A). In addition, the discontinuation rate among patients taking a restricted drug was higher than the non-restricted patients (model B). Furthermore, among the group of patients taking a restricted drug, the discontinuation rate was higher among patients aged 65 years or older (model C). In general, a lower discontinuation rate was associated with older patients, patients who had a prescription from a cardiologist, and previous non-adherence (gaps between prescription refills). Finally, as a test for sensitivity to model specification, a regression omitting the county control variable increased the magnitude of the PDL estimate on adherence from 82% higher odds to 92% higher odds (model not illustrated).

Discussion

Medicaid recipients taking statins in Alabama had an 82% higher risk of discontinuing therapy [odds ratio (OR) 1.82, 95% CI 1.57, 2.11] compared with North Carolina and with Alabama before the PDL. Patients taking unrestricted statins were also more likely to discontinue after the PDL (OR 1.44, 95% CI 1.16, 1.78). This could be related to the branded or total prescription limits or another unrelated cause. Those patients who were taking a restricted statin were more likely to discontinue after the PDL implementation than unrestricted statin patients (OR 1.42, 95% CI 1.12, 1.80). In addition, individuals aged 65 years or older who were taking a restricted medication were more likely to discontinue than their younger counterparts taking a restricted medication (OR 1.33, 95% CI 1.02, 1.73).[1]

[1] Recall that the *RESTRICTED* variable in our model indicates that the patient took atorvastatin, pravastatin, or rosuvastatin. In other words, if the patient took one of these three statins, then *RESTRICTED* = 1, even in Alabama before the PDL and in North Carolina where there were no such restrictions.

Table III. Additional characteristics of the patients in the sample[a]

State	PDL	n	% Aged 40–50 years	% Aged 51–64 years	% Aged 65+ years	% Male
Alabama	Pre-PDL	1664	12	24	44	22
	Post-PDL	1771	13	23	44	23
North Carolina	Pre-PDL	4520	12	20	50	26
	Post-PDL	5562	11	20	52	26

[a] At the start of the follow-up period.
PDL = preferred drug list.

Table IV. Proportion of patients switching drugs

State	PDL	n	% Switch	% Switch (restricted to non-restricted)
Alabama	Pre-PDL	1458	8	3
	Post-PDL	1666	50	47
North Carolina	Pre-PDL	3945	7	3
	Post-PDL	5086	9	3

PDL = preferred drug list.

Our estimates indicate that the PDL not only deterred patients from taking restricted statins but also deterred patients from taking unrestricted statins, perhaps because the unrestricted patients exceeded the Alabama limit of four brand-name prescriptions per month or ten total prescriptions per month. Given that Medicaid patients, particularly seniors, tend to have multiple chronic conditions, it is likely that some patients taking non-restricted drugs reached this limit.[43] In Alabama 4% of all Medicaid beneficiaries aged 45 years or older filled ten prescriptions or more per month and 20% filled five to ten prescriptions per month.[44] Even for patients below the limit, if the PDL limited access to another drug and discouraged the patient, she might fail to fill other prescriptions.

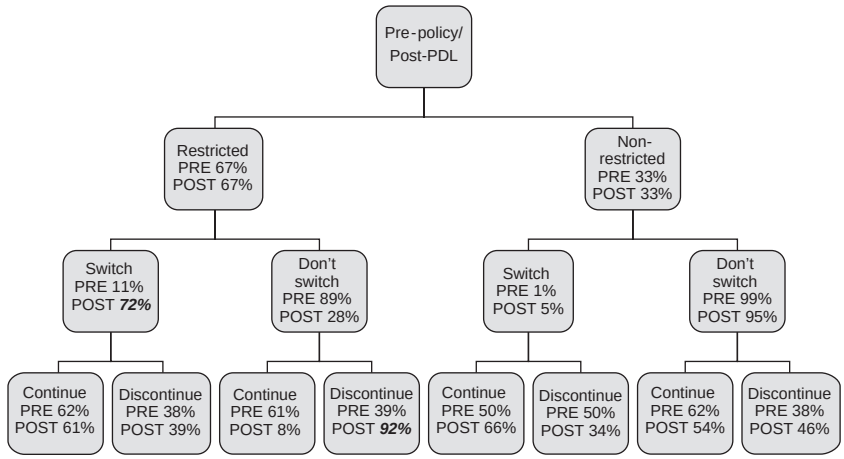

Fig. 2. Decision tree illustrating rates of discontinuation in Alabama. **PDL** = preferred drug list.

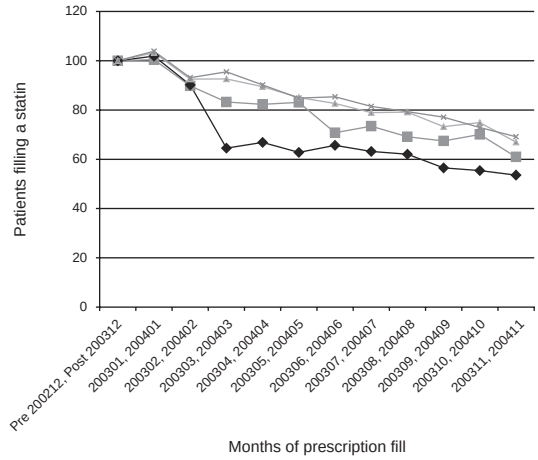

Fig. 3. Normalised number of patients filling a statin prescription by cohort in Alabama and North Carolina. —■— Alabama pre-policy; —◆— Alabama post-policy; —▲— North Carolina pre-policy; —×— North Carolina post-policy.

After the PDL implementation, a patient taking a restricted medication would arrive at the pharmacy to find that she was no longer able to fill a prescription for her medication. As the decision tree in figure 2 shows, a significant proportion of these patients did not switch to the preferred medication (28%), and nearly all of those patients discontinued treatment. Patients who did switch discontinued at approximately the same rate as the pre-PDL group. It is not known why some of the patients did not switch to the preferred medication. Perhaps their physician's office was overburdened by requests, the patient did not understand why the medication was not covered, or the physician asked the patient to come in for an appointment to adjust the medication. Notably, the discontinuation rate also increased, although to a lesser degree, in patients taking prescriptions that were not restricted.

The increase in the discontinuation rate for patients over the age of 65 years and taking restricted drugs is higher than the younger patients taking restricted drugs. There was no incremental effect from the PDL on any of the other patient age subgroups analysed. Because the elderly tend to have more chronic diseases and more expensive medical care, the effect of utilisation management tools such as PDLs should be monitored.

Since January 2006 (after the sample period for this study) disabled and aged Medicaid beneficiaries eligible for both Medicaid and Medicare ('dual eligibles') have switched to the Medicare Part D prescription drug benefit, which is administered by private insurers. The vast majority of these patients aged 65 or over are dually eligible for Medicare and Medicaid.[45] Medicaid

Table V. Logistic model predicting probability of discontinuation = 1

Variable	Model A		Model B		Model C	
	odds ratio	95% CI	odds ratio	95% CI	odds ratio	95% CI
PDL (Alabama in 2004)	1.82	(1.57, 2.11)*	1.44	(1.16, 1.78)*	1.44	(1.16, 1.79)*
RESTRICTED (rosuvastatin, atorvastatin, pravastatin)			0.98	(0.90, 1.07)	0.98	0.90, 1.07
PDL*RESTRICTED			1.42	(1.12, 1.80)*	1.26	0.97, 1.63
PDL*RESTRICTED*Age 65+					1.33	1.02, 1.73*
COUNTY fixed effects	Included	*	Included	*	Included	
Age 40–50	1.27	(1.10, 1.46)*	1.27	(1.10, 1.46)*	1.27	(1.10, 1.46)*
Age 51–64	0.94	(0.83, 1.06)	0.94	(0.83, 1.06)	0.94	(0.83, 1.06)
Age 65+	0.80	(0.72, 0.89)*	0.80	(0.72, 0.89)*	0.78	(0.70, 0.87)*
CARDIOLOGIST prescribed	0.66	(0.57, 0.77)*	0.66	(0.57, 0.77)*	0.66	(0.57, 0.77)*
PRIOR EXPERIENCE	0.99	(0.99, 0.99)*	0.99	(0.99, 0.99)*	0.99	(0.99, 0.99)*
PRIOR NON-ADHERENCE	4.80	(3.95, 5.84)*	4.84	(3.98, 5.88)*	4.84	(3.98, 5.88)*

* significant at $p < 0.01$. Likelihood ratio $B = 0 < 0.01$ for all models.
PDL = preferred drug list.

beneficiaries are enrolled together with higher-income beneficiaries in those privately administered insurance plans that have lower-than-average premiums. As such, dual eligibles and any other Medicare beneficiaries enrolled in their plans are subject to a host of cost containment measures (e.g. prescription limits, generic substitution, step therapy). Popular plans such as United Healthcare's AARP Prescription Rx requires prior authorisation for only few drugs, but Cigna's plan requires prior authorisation for 31 of the top 100 drugs in sales.[46] It is important to understand the impact of PDL implementation on patient behaviour to understand better how Medicare beneficiaries (both Medicaid and non-Medicaid alike) will respond to their new plans.

Heart disease is the leading cause of death nationwide.[28,29] Given that high cholesterol is a primary risk factor for heart disease, the cost management of medications that lower blood cholesterol should be undertaken carefully so as to not discourage treatment and prevention.

Limitations

The study is not a randomised-controlled trial. Our estimates will be biased by any changes coincident with the PDL implementation in Alabama but not in North Carolina. The study is retrospective and cross sectional. Multivariate analysis controls for several key variables that were available in the prescription claims, but does not control for co-morbid conditions, concurrent medications and patient–physician communication, which are not recorded on the prescription. Furthermore, limits on certain branded drugs were introduced simultaneously with limits on the number of perscriptions per month. This analysis does not separately estimate the effects. Therefore, the findings should be interpreted as estimating the effect of both policies on non-adherence.

The outcome measures in this study are calculated based on the claims captured in the set of pharmacies that continuously provided 100% of their data to Verispan during the entire study period. Prescriptions filled at multiple pharmacies were tracked and allocated to the patient via Verispan's encrypted identification process. However, if a patient used a pharmacy outside the sample that prescription was lost. This would bias the results if patients migrated to pharmacies outside the sample significantly more after the PDL in Alabama and they did not change their behaviour in North Carolina.

The sample of patients selected for this study is 6% larger in the post-PDL time period in Alabama and 23% larger in the post-PDL time period in North Carolina. There were no changes in eligibility criteria in 2004 in either state; the population enrolled in Medicaid increased by 3.5% in North Carolina and 4.1% in Alabama in June 2004 compared with the previous year.[47] There were no significant differences in any of the explanatory variables (age, time on therapy, sex, specialty of physician) in North Carolina that would indicate that the sample, although larger, was radically different in the post-PDL time period.

Not only would it be useful to have data on patient health status for control variables, but also for outcome variables. Previous researchers estimated the effects of drug access limits on short-term health outcomes. Such studies could, however, be inaccurate if there is a long lag between drug discontinuation and adverse health outcomes. In future research, one could assess the effect of the PDL on a marker such as cholesterol level. This would require access to patient charts or laboratory tests recorded before and after a policy change. The connections between access restrictions, therapeutic compliance, patient outcomes, and overall medical costs merit further research. Nevertheless, given the well-established benefits of statins[22–27] it is reasonable to be concerned that the PDL lowers the utilisation of statins, which might be detrimental to patient health.

Conclusions

There are at least two reasons why a state might adopt a PDL for a given therapy. First, a state might adopt a PDL if two drugs are therapeutically equivalent but priced differently, and benefit

managers expect that PDL implementation will not substantially decrease the use of an effective class of drugs. PDLs are socially good if the benefits from inducing patients to switch from a higher-cost statin to an equivalent but lower-cost statin exceed the costs in patient health and reduced incentives for innovation. Whether this occurs is an empirical question. Our evidence suggests that there was a substantial adverse effect on overall statin use. The health benefits of statins are well documented,[22–27] so it is not clear that the additional price savings justify the health consequences of decreasing the overall utilisation of statins.

On the other hand, a state might adopt a PDL in order to decrease pharmaceutical costs, even if it drives up other medical costs (e.g. hospital costs, long-term care costs), if someone else is paying the other costs. This 'silo' mentality occurs in at least three settings. First, before 2006, states were partly responsible for drug costs for low-income seniors through the Medicaid state–federal partnership, but were responsible for little of the overall medical costs for low-income seniors because those were paid by the federal government through Medicare. Second, since 2006, private insurers have been responsible for Medicaid dual eligibles, which includes qualifying disabled and seniors' drug bills through Medicare Part D, whereas the federal government is responsible for most of seniors' other medical costs (and the states are responsible for long-term care for poor seniors). Third, many private insurers pay for current prescription drug costs, but only expect to pay a fraction of future medical costs, because many patients change insurers and some die in the near future. Likewise, state officials might prefer to postpone healthcare costs until someone else is in office.

A PDL can be socially harmful if it has adverse consequences that the insurer did not anticipate or if the insurer does not care about adverse clinical and cost consequences that fall on other people or payers. In order to mitigate this 'silo' problem, the federal government could take two approaches. First, the Centers for Medicare and Medicaid Services (CMS) could influence the designs of Medicaid and Medicare prescription drug plans. They could be required to demonstrate that their medication utilisation management techniques do not decrease adherence with needed therapies, increase use of physician or hospital services or otherwise adversely impact long term costs or beneficiaries' health. Second, Medicare could encourage patients to enrol in Medicare Advantage plans, in which the private insurer is responsible for both drug and other medical costs.

Insurers and policy makers should be aware that seemingly benign limits can have unintended consequences for patient compliance with important medications. Although encouraging patients to switch between drugs might appear to save money, access restrictions may deter patients, especially vulnerable low-income patients, from adhering to important therapies, which could ultimately drive up long-term medical costs.

Acknowledgements

The authors are grateful for helpful comments from Amber Batata, Judith Kramer, Kimberly McGuigan, and the anonymous referees and editors. David B. Ridley was funded by Duke University. He has received grants from pharmaceutical companies in the past, but received no external funding related to this project. Kirsten Axelsen was funded by Pfizer Inc. The views expressed are those of the authors not Duke University or Pfizer Inc.

References

1. Centers for Medicare and Medicaid Services. History of the Medicaid drug rebate program [online]. Available from URL:http://www.cms.hhs.gov/MedicaidDrugRebateDispR/downloads/mdrphistory.pdf [Accessed 2006 August 9]
2. Kaiser Family Foundation. Prescription drug trends [online]. Available from URL: http://www.kff.org/rxdrugs/upload/3057-05.pdf [Accessed 2006 August 5]
3. Huskamp HA, Deverka PA, Epstein AM, et al. The effect of incentive-based formularies on prescription-drug utilization and spending. N Engl J Med 2003; 349 (23): 2224-32
4. Huskamp HA, Frank RG, McGuigan KA, et al. The impact of a three-tier formulary on demand response for prescription drugs. J Econ Managem Strategy 2005; 14 (3): 729-53
5. Joyce GF, Escarce J, Solomon MD, Goldman DP. Employer drug benefit plans and spending on prescription drugs. JAMA 2002; 288 (14): 1733-9

6. Manning WG, Newhouse JP, Duan N, et al. health insurance and the demand for medical care: evidence from a randomized experiment. Am Econ Rev 1987; 77 (3): 251-77
7. Motheral B, Fairman K. Effect of a three-tier prescription copay on pharmaceutical and other medical utilization. Med Care 2001; 39 (12): 1293-304
8. Rector TS, Finch MD, Danzon PM, et al. Effect of tiered prescription copayments on the use of preferred brand medications. Med Care 2003; 41 (3): 398-406
9. Ridley DB. Payments promotion and the purple pill. Duke University Working Paper. Durham: North Carolina, 2006
10. Texas Health and Human Services Commission. Medicaid cost sharing requirements: guidance for hospital emergency departments. November 26, 2002 [online]. Available from URL: http://www.hhsc.state.tx.us/medicaid/reports/Copay_EdMaterial/hospital.pdf [Accessed 2006 August 9]
11. Kaiser Commission on Medicaid and the Uninsured. State Medicaid outpatient prescription drug policies: findings from a national survey, 2005 update [online]. October 2005. Available from URL: http://www.kff.org/medicaid/7381.cfm [Accessed 2006 August 5]
12. Schwarzenegger RJ. Democrats agree on drug discount plan. Los Angeles Times. August 23, 2006 [online]. Available from URL:http://www.latimes.com/news/local/la-me-drugs23aug23,0,7427411.story [Accessed 2006 August 9]
13. Carroll NV. How effectively do managed care organizations influence prescribing and dispensing decisions? Am J Manag Care 2002; 8: 1041-54
14. National Association of Chain Drug Stores. Medicaid Prescription Drug and Dispensing Limits. October 2004 [online]. Available from URL: http://www.nacds.org/user-assets/pdfs/gov_affairs/issuebriefs/Medicaid%20Prescription%20Drug%20and%20Dispensing%20Limits%20%20October%202004.pdf [Accessed 2006 August 5]
15. Cunningham P, May J. Center for Studying Health System Change. Tracking report. Results from the Community Health Tracking Study. Number 16; August 2006
16. Soumerai SB, Ross-Degnan D, Avorn J, et al. Effects of Medicaid drug-payment limits on admission to hospitals and nursing homes. N Engl J Med 1991; 325 (15): 1072-7
17. Bloom B, Jacobs J. Cost effects of restricting cost-effective therapy. Med Care 1985; 23 (7): 872-80
18. Cromwell DM, Bass EB, Steinberg EP, et al. Can restrictions on reimbursement for anti-ulcer drugs decrease Medicaid pharmacy costs without increasing hospitalizations? Health Serv Res 1999; 33 (6): 1593-610
19. Smalley W, Griffin M, Fought R, et al. Effect of a prior authorization requirement on the use of nonsteroidal anti-inflammatory drugs by Medicaid patients. N Engl J Med 1995; 332 (24): 1612-7
20. Tamblyn R, Laprise R, Hanley JA, et al. Adverse events associated with prescription drug cost-sharing among poor and elderly persons. JAMA 2001; 285: 421-9
21. Wilson J, Axelsen K, Tang S. Medicaid prescription drug access restrictions: exploring the effect on patient persistence with hypertension medications. Am J Manag Care 2005; 11: SP27-34
22. Downs JR, Clearfield M, Weis S, et al. for the AFCAPS/TexCAPS Research Group. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. JAMA 1998; 279: 1615-22
23. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. Lancet 2003; 361:2005-16
24. The Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998; 339: 1349-57
25. Sacks FM, Pfeffer MA, Moye LA, et al. for the Cholesterol and Recurrent Events Trial Investigators. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. N Engl J Med 1996; 335: 1001-9
26. The Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994; 344: 1383-9
27. Shepherd J, Cobbe SM, Ford I, et al. for the West of Scotland Coronary Prevention Study Group. Prevention of coronary heart disease in men with hypercholesterolemia. N Engl J Med 1995; 333: 1301-7
28. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics – 2006 update. Circulation 2006; 113: e85-e151
29. Centers for Disease Control and Prevention. Profiling the causes of death in the United States. Heart disease, stroke and cancer. 2001 data [online]. Available from URL: http://www.cdc.gov/nccdphp/publications/factsheets/ChronicDisease/pdfs/Alabama.pdf [Accessed 2006 August]
30. Benner JS, Glynn RJ, Mogun H, et al. Long-term persistence in use of statin therapy in elderly patients. JAMA 2002; 288 (4): 455-61
31. Schultz JS, O'Donnell JC, McDonough KL, et al. Determinants of compliance with statin therapy and low-density lipoprotein cholesterol goal attainment in a managed care population. Am J Manag Care 2005; 11 (5): 306-12
32. Herper M. The world's best-selling drugs. Forbes. March 16, 2004 [online]. Available from URL: http://www.forbes.com/2004/03/16/cx_mh_0316bestselling.html [Accessed 2006 August 5]
33. Alabama Medicaid. Available from URL: http://www.medicaid.alabama.gov/programs/pharmacy_svcs/pa_overrides.aspx?tab=4 [Accessed 2006 August 5]
34. Kaiser Family Foundation. State Medicaid fact sheets [online]. Available from URL: http://www.kff.org/mfs/index.jsp [Accessed 2006 August 5]
35. United States Pharmacopeia. Comprehensive listing of drugs in the USP model guidelines [online]. Available from URL: http://www.usp.org/healthcareInfo/mmg/revisions.html [Accessed 2005]
36. Card D. Do minimum wages reduce employment? a case study of California, 1987–89 Indust Labor Relat Rev 1992; 46: 38-54

37. Gruber J. The incidence of mandated maternity benefits. Am Econ Rev 1994; 84: 622-41
38. Steiner JF, Prochazka V. The assessment of refill compliance using pharmacy records: methods, validity, and applications. J Clin Epidemiol 1997; 50: 105-16
39. Ellis JJ, Erickson SR, Stevenson JG, et al. Suboptimal statin adherence and discontinuation in primary and secondary prevention populations. J Gen Intern Med 2004; 19: 638-45
40. Gibson TB, Mark TL, McGuigan K, et al. The effects of prescription drug co-payments on statin adherence. Am J Manag Care 2006; 12 (9): 509-17
41. US Census Bureau [online]. Available from URL: http://quickfacts.census.gov/qfd/states/ [Accessed 2006 August 5]
42. Kaiser Family Foundation. State Medicaid fact sheets. Available from URL: http://www.kff.org/mfs/index.jsp [Accessed 2006 August 5]
43. Fortess EE, Soumerai SB, McLaughlin TJ, Ross-Degnan D. Utilization of essential medications by vulnerable older people after a drug benefit cap: importance of mental disorders, chronic pain, and practice setting. J Am Geriatr Soc 2001; 49: 793-7
44. Centers for Medicare and Medicaid Services. MAX 1999 file for Alabama, released by CMS in January 2004
45. Kaiser Commission on Medicaid and the Uninsured. Dual eligibles: Medicaid's role for low-income medicare beneficiaries; January 2006
46. Frakt AB, Pizer SD. A first look at the new Medicare prescription drug plans. Health Affairs 2006; 25 (4): 252-61
47. Kaiser Commission on Medicaid and the Uninsured. Medicaid enrollment in 50 states, June 2004 data update; September 2005

Correspondence and offprints: *David Ridley*, Duke University, The Fuqua School of Business, Box 90120, Durham, North Carolina, USA.
E-mail: david.ridley@duke.edu