ORIGINAL RESEARCH

Evaluation of Product Switching After a State Medicaid Program Began Covering Loratadine OTC 1 Year After Market Availability

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ABSTRACT

OBJECTIVE: The conversion of loratadine from prescription (Rx)-only to over-the-counter (OTC) status on November 27, 2002, brought about the question of how OTC products may influence utilization of both OTC and Rx-only low-sedating antihistamines (LSAs) simultaneously. North Carolina (NC) Medicaid initially did not cover loratadine OTC but subsequently changed the policy 1 year after OTC conversion, on November 23, 2003. The objective of this study was to determine patterns of LSA utilization in relation to changes in OTC availability and Medicaid coverage policy and to assess the rate of product switching associated with these policies.

METHODS: Administrative pharmacy claims from the NC Medicaid population of approximately 1.1 million eligible recipients were used to study the 3 years of LSA use between July 1, 2001, and June 30, 2004. Two general methods were employed to evaluate the extent of product switching. First, monthly rates of incident use, new starts (i.e., no LSA use in the prior 12-month period) and product switching in time series were determined. These series were constructed to include a baseline period of no OTC availability, a period of OTC availability without coverage, and a period of OTC availability with coverage. Second, product switching was assessed through the use of rate-ratio calculations. Three equal 12-month periods were compared using rate ratios: (1) a baseline referent period (July 1, 2001, to June 30, 2002) during which loratadine OTC was not yet available, (2) a noncoverage period (July 1, 2002, to June 30, 2003) during which loratadine OTC was introduced to the market but not covered by NC Medicaid, and (3) a coverage period (July 1, 2003, to June 30, 2004). The primary comparison periods for the 3 years were the 5-month periods from February to June of each year.

RESULTS: The use of individual drugs within the LSA class responded to coverage changes as expected, with alternative LSAs replacing loratadine use in the loratadine noncoverage period. Switching behavior for individual drugs within the LSA class was strongly associated with coverage changes. Recipients using loratadine were 2.16 times more likely to switch to an alternative Rx-only antihistamine in the noncoverage period (95% confidence interval [CI], 2.10-2.22) as compared with the baseline period. Yet they were only 1.11 times as likely not to use an Rx LSA during the last 5 months of the noncoverage period (95% CI, 1.09-1.13), as compared with the baseline period, suggesting minimal OTC uptake. The largest 12-month percentage increase in market share was observed for cetirizine (13.4%) although desloratadine accounted for the largest switch rate from loratadine at 3.10 (95% CI, 2.91-3.30), as compared with the baseline period, with a total market share increase of 7.8%. This suggests that new users of LSAs were most likely to initiate therapy with cetirizine, while existing loratadine users were most likely to switch to desloratadine. Compared with baseline switch rates, LSA users were only 0.34 (95% CI; 0.32-0.37) times as likely to switch to loratadine OTC from another (Rx-only) LSA during the subsequent OTC coverage period. LSA expenditure per member per month (PMPM) was essentially constant over time, at $3.03 in the 5-month pre-OTC period, $2.96 in the 5-month loratadine noncoverage period, and $2.93 in the 5-month coverage period for loratadine OTC. Total LSA utilization increased slightly, from 1.37 days PMPM in the 5-month pre-OTC period to 1.41 in the 5-month loratadine noncoverage period and 1.45 in the 5-month coverage period for loratadine OTC. Loratadine OTC accounted for only 4.1% of the total LSA days of therapy and 4.2% of the LSA patients in the 5-month OTC coverage period from February to June 2004.

CONCLUSION: Medicaid recipients switched to another covered (Rx) LSA when loratadine became available as an OTC and was not covered. After the subsequent policy change 1 year later to cover loratadine OTC, there was little switching to loratadine OTC. Though the average cost per LSA claim dropped $4.15 (6.6%), from $62.79 in the baseline period to $58.64 in the OTC coverage period, time-series and rate-ratio results suggest that an additional $6.01 (10.2%) could have been saved per LSA claim had OTC coverage been in effect at the time of the conversion of loratadine to OTC status. Although coverage of loratadine OTC offers a substantial cost-savings opportunity for the Medicaid program compared with Rx-only LSAs, not covering the OTC product immediately at the time of OTC availability contributed to (a) increased switching to Rx-only LSA products and (b) little use of loratadine OTC in the subsequent OTC coverage period.

KEYWORDS: Loratadine, Medicaid, Over the counter, OTC, Low-sedating antihistamine, LSA, Drug utilization, Switching

J Manag Care Pharm. 2006;12(2):108-20

Since the introduction of loratadine (Claritin) in 1993, expenditures on low-sedating antihistamines (LSAs) have accounted for a significant portion of prescription (Rx) drug spending. Oral antihistamines accounted for more than $5.1 billion[1] (approximately 4.0%) of total community pharmacy sales in the United States in 2001, ranking ninth among all drug classes.[2] On November 27, 2002, the U.S. Food and Drug Administration (FDA) approved loratadine as the first-ever LSA for over-the-counter (OTC) sale.[3] Loratadine was officially introduced to the OTC market in December 2002, first marketed as Claritin and Alavert (Wyeth Consumer Healthcare) and subsequently under several label names.

Following OTC approval, many private health plans responded by moving loratadine to the highest copayment tier or by removing loratadine from coverage in the pharmacy benefit.[4] For state Medicaid programs, benefit design is largely determined at the state level, and there is wide variability in OTC coverage, types of drugs covered, and copayment amounts among the states.[5,6] At the time of initial OTC marketing of loratadine in 2002, 31 states had partial coverage of OTC antihistamines, and 19 states had some form of prior authorization for Rx antihistamines.[6] For those states not covering OTC products, loratadine OTC was removed from the pharmacy benefit altogether. Since copayments for Medicaid recipients are generally nominal, a covered Rx-only alternative almost always costs less out of pocket than a comparable OTC product at retail cost, creating an incentive for the Medicaid recipient to use a more expensive Rx-only product.

In the case of the OTC conversion of loratadine Rx, the Rx version of the drug was removed completely from the market.[4] This is in contrast with other OTC conversions in which availability was tied to strength (as with histamine-2 blockers and

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nonsteroidal anti-inflammatory agents in which lower-strength products were OTC and higher-strength products continued to be available by Rx) or chemical moiety (as with omeprazole magnesium). Therefore, in the Rx-to-OTC conversion of loratadine, there was no dual OTC and Rx market existence. Thus, pharmacy benefit plans that did not cover OTC products were left with 2 options: (1) drop loratadine from the pharmacy benefit or (2) initiate coverage of OTC products in general or loratadine OTC as an exception.

Either of these options may result in drug cost savings relative to pre-OTC availability. One study using decision analysis to model the budgetary impact of Medicaid policies following the loratadine OTC conversion reported a $.02 per-member-per-month (PMPM) savings for coverage.[7] A separate analysis from a societal perspective found that availability of LSAs over the counter would be associated with annual savings of $4 billion, or $100 dollars per allergic rhinitis sufferer per year, and 135,061 time-discounted quality-adjusted life-years.[8]

Another study modeled the impact of discontinuing OTC coverage in the Oregon Medicaid program. Using a time-series analysis to evaluate the 1993 policy change, the authors concluded that eliminating OTC coverage reduced program costs, with limited evidence of substitution to Rx-only products.[9] Empirical evidence from a study considering a number of different managed care pharmacy benefit plans found that the Rx-to-OTC switch of loratadine resulted in a decrease in all allergic rhinitis-related utilization, suggesting that the decrease in LSA utilization was not associated with a commensurate increase in use of other allergic rhinitis drugs such as nasal steroids or montelukast.[10] However, none of these studies reflects the specific effect within a Medicaid environment, and none directly assesses loratadine OTC coverage or its use. In fact, Sullivan et al. point to the inability to readily measure OTC use as a serious limitation that needs to be addressed in future papers.[10]

The study of concurrent OTC and Rx drug use will become increasingly important as more drugs become available over the counter. Nearly 4 out of every 5 Americans report using an OTC product in the previous 6 months,[11] and nearly two thirds of all OTC purchases in 1996 were for products containing ingredients that were once Rx-only.[12] Studying the transition and subsequent use of formerly Rx-only products is becoming essential to understanding overall drug use in member populations.

The opportunity costs associated with noncoverage of OTC products is of interest to all benefit managers, regardless of payer type. Despite the studies that have suggested reductions in payer cost associated with the marketing of OTC products, none have examined the opportunity costs associated with not covering OTC products. Benefit managers and health plan sponsors are interested in determining if and by how much plan benefit dollars can be saved by noncoverage of OTC drugs versus coverage of OTC drugs. This determination is becoming more important given the OTC conversions of costly drugs such as omeprazole OTC (Prilosec) and the recent consideration of OTC availability of select statins.[13]

The State Employee Health Plan of North Carolina (NC) likely considered this matter when redesigning the benefit structure for proton pump inhibitors (PPIs) for state employees. The customary $10 generic copayment was reduced to $5 for omeprazole OTC to create a financial incentive for its use.[14] Evidence of the value of OTC coverage was produced by the study of the Arkansas State Employee Health Plan, which added coverage of omeprazole OTC at a reduced copayment. Coverage of omeprazole OTC resulted in 47% market share for the OTC drug in the first week of the policy change, with a consequent cost reduction to the state of approximately 50% for the entire PPI class of drugs.[15]

Historically, Medicaid coverage of OTC products was extended only to insulin in NC. Hence, when loratadine was approved for OTC sale, NC Medicaid recipients were no longer able to obtain it as a covered benefit except for existing pharmacy stock of loratadine Rx, which could be dispensed and reimbursed. When the pharmacy stock of loratadine Rx was depleted, NC Medicaid recipients taking loratadine had 3 options: (1) obtain an Rx for an alternative covered product such as cetirizine (Zyrtec), desloratadine (Clarinex), or fexofenadine (Allegra); (2) purchase the OTC product out of pocket; or (3) stop using an LSA. Given the higher cost of the OTC product ($8-$15) relative to the $3.00 copayment for the branded Rx LSA in the Medicaid pharmacy benefit at the time, it is likely that most NC Medicaid recipients switched to a covered Rx-only LSA. Approximately 1 year following OTC availability, NC Medicaid changed its OTC policy to cover select products, including loratadine OTC on November 23, 2003, citing both access and potential cost savings.[16]

The present study takes advantage of the natural timing of these 2 policy changes: the FDA approval of loratadine OTC in late November 2002 and the approval of coverage of loratadine OTC in the state Medicaid program the next year, in November 2003. In the private sector, the conversion of loratadine from an Rx-only to an OTC product greatly increased access to the drug for individuals who can afford the OTC price and also made a physician visit unnecessary to obtain the drug. For NC Medicaid recipients, however, this change caused an increase in out-of-pocket costs since OTC products were not included as a pharmacy benefit (loratadine Rx had a $3.00 copayment before OTC conversion). One year after OTC conversion, a change in NC Medicaid drug policy allowed OTC products to be covered for a copayment of $1.00 per claim.

Given the potential drug cost savings of loratadine OTC, the effect of NC Medicaid coverage policies on LSA utilization and product switching was evaluated. Despite coverage of loratadine 1 year after its OTC conversion, failing to cover the product at the time of conversion may have diminished those

savings through increased product switching. This hypothesized effect was evaluated by (1) determining the patterns of LSA utilization in relation to changes in OTC availability and coverage policy and (2) assessing the rate of LSA product switching as a function of OTC availability and coverage policy.

Methods

A retrospective analysis of pharmacy claims was undertaken for the NC Medicaid program for the 3-year period from July 1, 2001, through June 30, 2004. This period includes both the federal policy change (OTC conversion on November 27, 2002) and the state policy change (loratadine OTC coverage on November 23, 2003). Specifically, the following products were considered in the present analysis: loratadine Rx, loratadine OTC, cetirizine, desloratadine, and fexofenadine. During the period of this study, there was no mail-service pharmacy option available to NC Medicaid recipients, and there was a supply limit of 34 days per community pharmacy claim.

Two general methods were employed to evaluate the extent of product switching. First, we determined 3 types of monthly rates in time series: aggregate LSA use (the total number of respective LSA claims), incident LSA starts (the number of enrollees initiating an LSA following a year of nonuse), and incident product switching (the number of enrollees switching from loratadine Rx to another LSA following a year of exclusive loratadine Rx use). These monthly rates were used to construct time series that were inclusive of both federal and state (Medicaid) policy changes over the 3-year study period. This approach provided a qualitative illustration of the effect of these policy changes on utilization patterns and switching behavior but did not allow statistical testing due to limitations associated with the use of time-series analysis. To overcome this limitation, the second approach employed the construction of rate ratios to quantify product switching. Year-long rates of switching among 3 discrete periods were compared: (1) a baseline period of no policy changes, (2) an OTC noncoverage period, and (3) an OTC coverage period.

Each of the 3 time series provided a separate but necessary component of the overall analysis to determine the effect of policy changes. Monthly aggregate (all) LSA use was used to determine general trends in total LSA use that could be linked directly to each policy change. However, since this time-series method could not parse out the specific effect of policy changes between new users and product switchers, incident LSA starts (at least 1 year of prior nonuse) and incident product switching were determined to separate the effect of coverage changes for new LSA users from the effect of coverage changes on existing LSA users.

Monthly aggregate LSA use was calculated from the total number of paid LSA claims per 1,000 eligible recipients per month for the time period from July 1, 2001, to June 30, 2004. Over this 3-year period, the number of Medicaid recipients increased from 990,000 to 1.1 million. Thus, an analysis of 1,000 recipients was employed to normalize the growth in number of eligible recipients over time. Utilization was defined as paid pharmacy claims for any quantity, strength, or dosage of LSAs, regardless of Medicaid recipient eligibility.

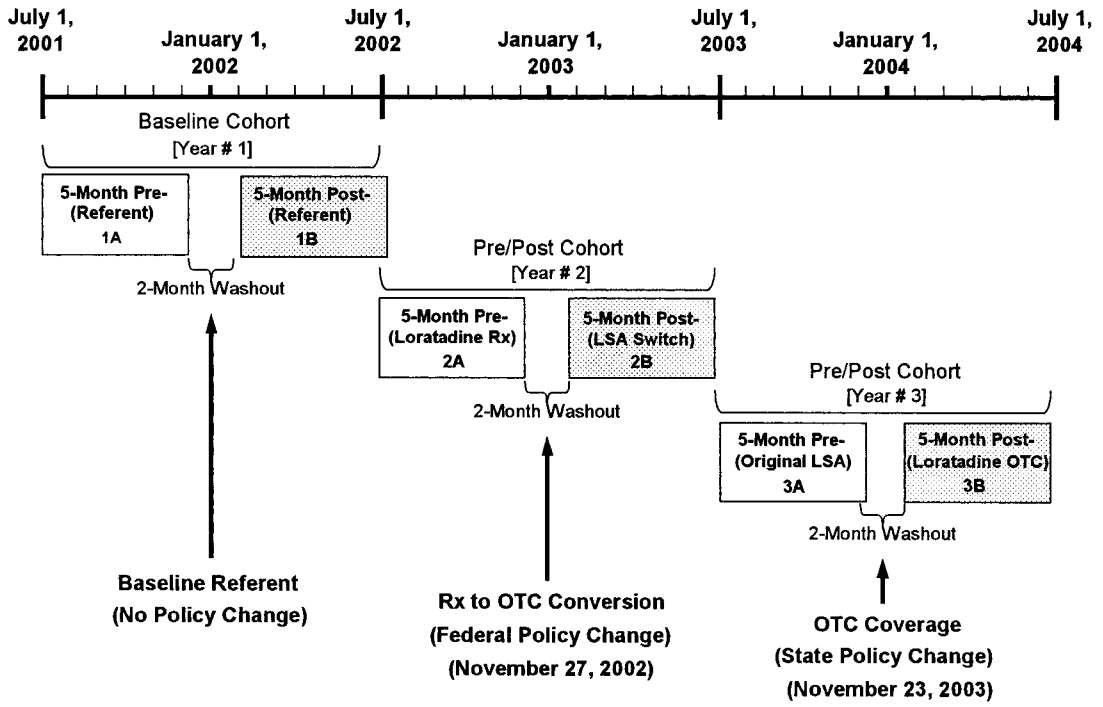
To assess the frequency and product distribution of incident LSA starts over time, LSA starts per 1,000 nonusers (no LSA use) per month were calculated. Since LSAs are often used on an as-needed basis and seasonal utilization of LSAs is common, incident LSA starts were determined by 1 year of nonuse. Enrollees were considered nonusers if, prior to initiating LSA use, no LSA claim had been filed in the year prior to that LSA pharmacy claim. Continuous Medicaid eligibility was not required for these analyses since this requirement would have reduced the study population by almost half. Monthly LSA starts are reported for the period from January 2002 through June 2004, and claim data spanning the 12-month period from January 2001 through December 2001 were used to determine nonuse for the monthly rates in January 2002, with subsequent 1-year run-in periods to determine nonuse for respective monthly rates.

To assess product switching, the number of enrollees switching from loratadine Rx to other LSAs per 1,000 loratadine Rx users per month was calculated over time. A loratadine Rx user was required to have a 1-year run-in period of exclusive loratadine Rx use. As was the case with the new-start classification, continuous eligibility was not required to be considered a loratadine Rx user due to the transient eligibility commonly found with Medicaid recipients. Rather, loratadine Rx users were defined as those recipients having any eligibility in the prior 12 months, with no LSA claim other than at least 1 claim for loratadine Rx. Subsequent 1-year run-in periods of exclusive loratadine Rx use were used to determine the denominator for each monthly rate, and the numerator was determined from the LSA product switches in the respective months.

While the time-series approach provides a good visual depiction of switching behavior over time, it does not show clearly the specific magnitude of the policy effect. Furthermore, traditional statistical modeling techniques typically employed with time-series analysis are limited in that they require significant longitudinal history[17] and are often difficult for policy makers to interpret.[18] Therefore, the rate-ratio method was employed as a second, adjunct approach to compare the rate of product switching between both exposure periods (noncoverage and coverage) and the baseline referent period. This approach also has been used to characterize the seasonality of emergency department visits for asthma in schoolchildren.[19]

This rate-ratio method of quantification was also necessary for precision and for testing for statistical significance. More importantly, this approach also enabled use of LSA persistence as a proxy for OTC use in the absence of claims for OTC products during the noncoverage period. Specifically, this was achieved

FIGURE 1 Before-After Cohort Strategy for Rate Ratio Construction



Period 1A = All loratadine Rx users in the first 5 months of the referent period (Jul.-Nov. 2001).
Period 1B = LSA users who switched from loratadine Rx to another LSA in the referent period (Feb.-Jun. 2002).
Period 2A = All loratadine Rx users in the first 5 months of the OTC noncoverage period (Jul.-Nov. 2002).
Period 2B = LSA users who switched from loratadine Rx to another LSA in the OTC noncoverage period (Feb.-Jun. 2003).
Period 3A = All Rx LSA users in the first 5 months of the coverage period (Jul.-Nov 2003).
Period 3B = Users who switched from an Rx LSA to loratadine OTC in the coverage period (Feb.-Jun. 2004).

LSA=low-sedating antihistamine; OTC=over the counter; Rx=prescription.

by determining the number of persons who did not persist in LSA use across each policy period. With a rate-ratio approach, rates of baseline discontinuation (persistence) are canceled out by the division of rates from both the referent-baseline and the policy periods. The definition of LSA discontinuation for the purposes of this analysis was the absence of a pharmacy claim for an LSA during the period of interest. Thus, an LSA persistence rate ratio of 1.0 indicates constant baseline LSA discontinuation over time, whereas a rate ratio greater than 1.0 indicates 1 of 2 possible scenarios: (1) increased discontinuation or (2) OTC uptake. The magnitude of change is multiplicative. Thus, a rate ratio of 2.0 results from a 2-fold increase in LSA discontinuation in the exposure period (OTC noncoverage) versus the baseline period (referent). The validity of this ratio with respect to policy attribution is dependant on the absence of confounding factors While this assumption is an important limitation, it is common to all quasi-experimentation in policy analysis, especially time-series applications.

Using the rate-ratio approach, switching behavior was measured for 3 different 12-month time periods, using the natural timing of OTC conversion and changes in NC Medicaid OTC coverage. In each 12-month period, switch rates were calculated by comparing LSA users in the first 5 months of the year-long period with LSA users in the last 5 months of the year-long period. The first 5 months of each year-long period were used to identify LSA users and classify eligible users according to which LSA(s) they used. The last 5 months of each period were used to compare changes in LSA utilization with prepolicy use; an LSA switcher was defined as an LSA user with an LSA product change.

Exclusive use of a given product was required, meaning that a Medicaid recipient with a pharmacy claim for more than 1 type of LSA (e.g., cetirizine and fexofenadine) was excluded from the data when calculating the rate ratios. Requiring mutual exclusivity ensured that comparisons could be made across

EQUATION 1 *Rate Ratio for Switching in the OTC Noncoverage Period Compared With the Referent Period*

$$\frac{\dfrac{\text{LSA users who switched from loratadine Rx to another LSA in the OTC noncoverage period (Feb.-Jun. 2003)}}{\text{All loratadine Rx users in the first 5 months of the OTC noncoverage period (Jul.-Nov. 2002)}}}{\dfrac{\text{LSA users who switched from loratadine Rx to another LSA in the referent period (Feb.-Jun. 2002)}}{\text{All loratadine Rx users in the first 5 months of the referent period (Jul.-Nov. 2001)}}} = \frac{\frac{2B}{2A}}{\frac{1B}{1A}}$$

EQUATION 2 *Rate Ratio for Switching to Loratadine OTC in the Coverage Period Compared With the Referent Period*

$$\frac{\dfrac{\text{Users who switched from an Rx LSA to loratadine OTC in the coverage period (Feb.-Jun. 2004)}}{\text{All Rx LSA users in the first 5 months of the coverage period (Jul.-Jun. 2002)}}}{\dfrac{\text{Users who switched from an Rx LSA to loratadine Rx in the referent period (Feb.-Jun. 2002)}}{\text{All Rx LSA users in the first 5 months of the referent period (Jul.-Nov. 2001)}}} = \frac{\frac{3B}{3A}}{\frac{1B}{1A}}$$

LSA = low-sedating antihistamine; OTC = over the counter; Rx = prescription.

drug products and that the number of switchers for each type of drug product added up to the sum total of LSA switchers

In each exposure period, the 5-month intervals were centered over the spring and fall, the peak seasons of LSA use. The middle 2 months (December and January) were used as a washout interval when pharmacy claims were not evaluated. Both policy changes occurred at the end of the month of November, immediately before the beginning of the washout interval. The purpose of the washout interval was 2-fold: (1) to account for minimal differences in the timing of market and policy changes within the periods (loratadine was approved for OTC status on November 27, 2002,[3] and Medicaid coverage of loratadine OTC began on November 23, 2003) and (2) to allow for policy uptake. In the case of OTC noncoverage, time was needed for patients to get an Rx to switch to alternative products. For the OTC coverage period, the washout interval provided a lag time to allow the OTC product to get to market in sufficient supply (e.g., the first 3 National Drug Code [NDC] numbers to become available for online adjudication occurred for loratadine 10 mg tablets on November 25, 2003, December 19, 2003, and January 8, 2004[20]).

For the calculation of the rate ratios, the first 12-month period (July 1, 2001-June 30, 2002) was used as a reference (the referent, or baseline, period) (Figure 1). The second 12-month period (July 1, 2002-June 30, 2003) was the period of loratadine OTC availability without coverage by NC Medicaid (the OTC noncoverage period). The final 12 months (July 1, 2003-June 30, 2004) represented a period of loratadine OTC coverage by NC Medicaid (the OTC coverage period). Each period comprised the same calendar months (July-June) in an attempt to account for the seasonality of LSA claims.

The first rate-ratio calculation (Equation 1) compared the rate of switching in the OTC noncoverage period with the rate of switching in the referent period. Note that the numerators and denominators of this equation are seasonally equal, 5-month intervals with equal 2-month washout intervals to a total 1-year period for each policy. [July-November] + [December-January] + [February-June] = 12 months. Specifically, the comparison was the rate of switching from loratadine Rx to another LSA or stopping use of an LSA altogether (i.e., nonuse). As previously mentioned, the term nonuse describes the absence of an LSA claim in the period of interest. More specifically, the nonuse classification includes 2 types of Medicaid recipients: (1) true nonusers and (2) users who purchased loratadine OTC on their own. By constructing a rate ratio comparing nonuse in different policy periods, the baseline discontinuation that frequently occurs with as-needed products such as LSAs is cancelled out. Thus, if the rate of recipients discontinuing Rx-only LSA use is larger in the policy period than in the referent period, the increased discontinuation in pharmacy claims may be attributed to the policy change at hand. Subsequently, the rate ratio represents the multiplicative magnitude of combined (1) loratadine OTC uptake and (2) class-wide LSA discontinuation regardless of legend (Rx or OTC) status. This method alone does not allow parsing the dominant effect. This approach does, however, help overcome the confounding of OTC use not accounted for in pharmacy claims.

Under the null hypothesis, the rate ratio should be equal to 1.0 if no NC Medicaid recipients were purchasing an OTC product on their own following the availability of loratadine OTC. Rate ratios greater than 1.0 indicate increased switching to the nonuse category. More specifically, rate ratios greater than 1.0 indicate either greater discontinuation of LSA products after the policy change or initiation of self-purchased OTC use. Determining which of these scenarios dominates is beyond the capability of this method although one may refer to the analysis of aggregate LSA utilization in time series (as well as LSA starts) to confirm persistence and constancy of overall LSA use. If aggregate LSA use remained constant over time, one might infer that no OTC uptake occurred when the resultant discontinuation (persistence) rate ratio is 1.0.

The second set of rate ratios was designed to represent the degree to which recipients using an Rx-only LSA switched to loratadine OTC once OTC coverage was implemented. The numerator is the rate of persons switching from an Rx-only LSA to loratadine OTC after OTC coverage became effective (in November 2003). A rate for new LSA starts was also determined (nonuse to loratadine OTC use). To be consistent and to permit inclusion of more data, the "any eligibility" criterion used for the time-series approach was also used for these rate-ratio calculations. Thus, for any categorization in any period of interest, only 1 month of eligibility was required for inclusion. For the denominator, the referent-baseline period (July 1, 2001-June 30, 2002) was used to compare the rate of switching to loratadine Rx versus switching to loratadine OTC (Equation 2). In other words, the switch rates were assumed to be equal, both practically and in theory, since loratadine OTC was the same chemical entity as the Rx-only product (i.e., same dosage, formulation, etc.). Thus, differences in switching should be primarily related to coverage.

As before, rate ratios greater than 1.0 represent more switching to loratadine OTC in a period of coverage versus switching to loratadine Rx in a referent period. Ratios less than 1.0 reflect less use of the OTC product as compared with baseline switching patterns with the Rx product. Ratios equal to 1.0 would imply no difference in loratadine OTC uptake versus loratadine Rx uptake.

Desloratadine was introduced to the market in January 2002 (FDA-approved on December 21, 2001)[3] and was not available to the U.S. market during the referent-baseline period. Therefore, it was not possible to calculate rate ratios for switching from desloratadine to loratadine OTC.

Chi-square tests and corresponding 95% confidence intervals [CIs] were calculated to compare the rate of switching for each drug. All data management and statistical testing was performed using Statistical Analysis Software, SAS version 9, Cary, NC.

Results

Over the 3-year study period, NC Medicaid accumulated 1.7 million pharmacy claims for LSAs, totaling $106 million for 377,722 recipients. The prevalence of LSA use was 4.7% of eligible Medicaid recipients in the 5-month pre-loratadine OTC period from February through June 2002 and 4.8% in each of the latter 2 periods, from February through June 2003 (the loratadine OTC noncoverage period) and February through June 2004 (the loratadine OTC coverage period) (Table 1). The mean age as of the first claim on file during the study period was 26 years, whereas the median age was 15 years. Nearly two thirds (63.31%) were female, and 94.1% were community-dwelling Medicaid recipients. The remaining 5.9% of eligible recipients were in institutional care, including domiciliary care and mental hospital care. The days supply limit (34) was the same for institutional care recipients as for community-dwelling recipients.

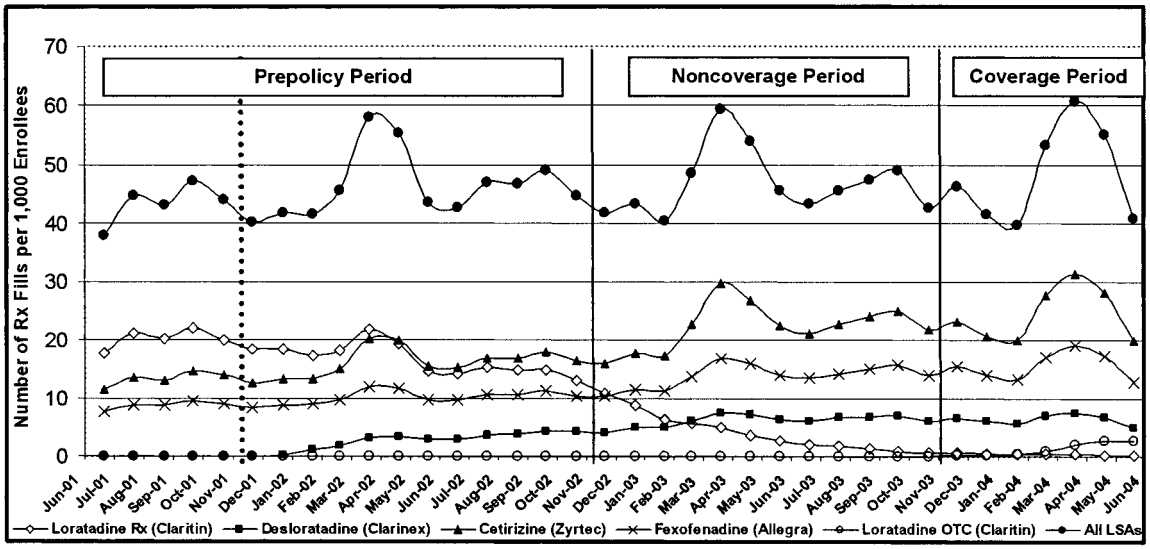
LSA use remained steady and seasonal, with remarkable predictability throughout the 3-year study period. The highest use was observed during the months of April and May, peaking

TABLE 1 *LSA Utilization and Cost for the 3 Measurement Periods*

	Pre-OTC Period (Feb.-Jun. 2002)	Noncoverage Period (Feb.-Jun. 2003)	OTC Coverage Period (Feb.-Jun. 2004)
LSA Rxs	243,857	262,426	276,329
LSA days	6,906,738	7,498,730	7,991,652
LSA patients	47,088	50,529	53,281
LSA expenditures	$15,311,733	$15,698,614	$16,205,124
Loratadine Rxs	92,906	24,447	11,453
Loratadine days	2,657,009	706,199	330,122
Loratadine patients	18,107	4,798	2,233
Loratadine expenditures	$7,185,016	$2,172,901	$233,932
Eligible member-months	5,057,242	5,312,670	5,529,713
LSA days/Rx	28.3	28.6	28.9
Loratadine days/Rx	28.6	28.9	28.8
Loratadine Rx %	38.1%	9.3%	4.1%
Loratadine days %	38.5%	9.4%	4.1%
Loratadine patients %	38.5%	9.5%	4.2%
Loratadine dollar %	46.9%	13.8%	1.4%
Avg. LSA cost per day	$2.22	$2.09	$2.03
Avg. loratadine cost per day	$2.70	$3.08	$0.71
Avg. cost per LSA Rx	$62.79	$59.82	$58.64
Avg. cost per loratadine Rx	$77.34	$88.88	$20.43
Prevalence of LSA use	4.7%	4.8%	4.8%
LSA days PMPM	1.37	1.41	1.45
LSA expenditures PMPM	$3.03	$2.96	$2.93

LSA=low-sedating antihistamine; OTC=over the counter; PMPM=per member per month; Rx=prescription.

FIGURE 2 *Aggregate Monthly LSA Use per 1,000 Enrollees by Drug*



LSA=low-sedating antihistamine; OTC=over the counter; Rx=prescription.

TABLE 2 *Switch Rates and Rate Ratios for the Comparison of the OTC Noncoverage Period With the Referent (Baseline) Period*

		Period			
		Referent (Baseline) Jul.-Nov. 2001 → Feb.-Jun. 2002	Rx to OTC Conversion (OTC Noncoverage) Jul.-Nov. 2002 → Feb.-Jun. 2003		
Switch from	Switch to	Rate/1,000*	Rate/1,000*	Rate Ratio	95% CI for Rate Ratio
Loratadine (Rx)	No LSA	466	517	1.11‡	1.09-1.13
Loratadine (Rx)	Another LSA†	139	300	2.16‡	2.10-2.22
Loratadine (Rx)	Cetirizine	66	129	1.95‡	1.87-2.05
Loratadine (Rx)	Desloratadine	30	93	3.10‡	2.91-3.30
Loratadine (Rx)	Fexofenadine	43	78	1.82‡	1.72-1.93

** Rate/1,000 is defined as the number of switch events per 1,000 eligible users. For this table, eligible users are loratadine users in the 5-month preinterval of both the referent-baseline period (n=44,115 for Jul.-Nov. 2001) and the noncoverage period (n=30,955 for Jul.-Nov. 2002).*

†Another LSA refers to the combination of switches to the covered drugs: cetirizine, desloratadine, or fexofenadine.

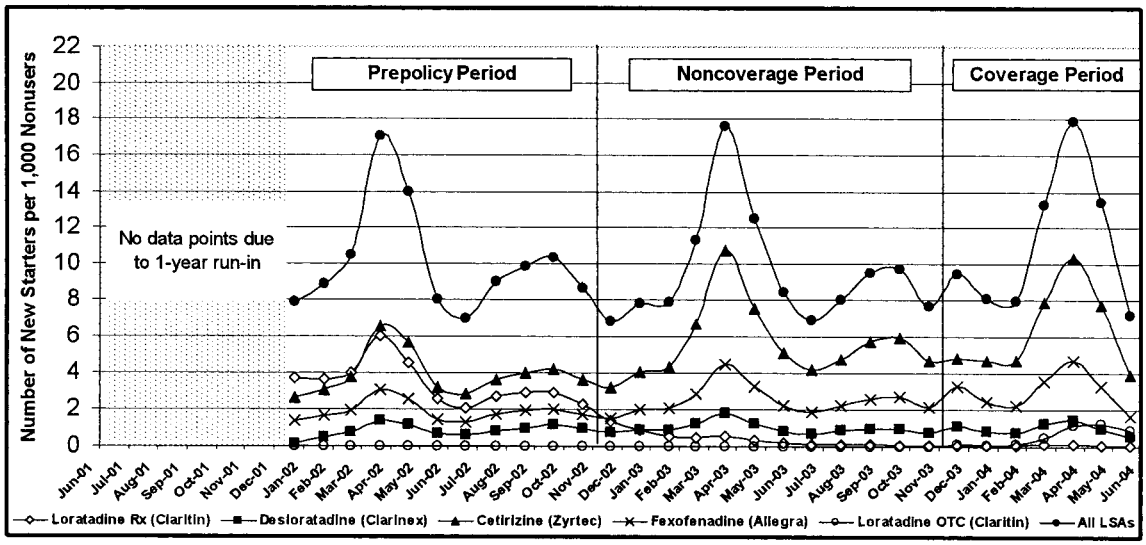
‡ P <0.001 for chi-square test of the null hypothesis that the rate of switching in the referent period was the same as the rate of switching in the Rx to OTC noncoverage period.

CI=confidence interval; LSA=low-sedating antihistamine; OTC=over the counter; Rx=prescription.

at approximately 60 pharmacy claims per 1,000 eligible Medicaid enrollees every spring (Figure 2). A fall peak was found in the month of October, with approximately 50 pharmacy LSA claims per 1,000 eligible Medicaid enrollees. In general, LSA use varied between 40 and 60 pharmacy claims per 1,000 recipients, with no apparent upward trend. This occurred despite a dramatic shift in market share for cetirizine and the market introduction of desloratadine.

New LSA starts also were steady, with remarkable seasonal predictability. A surge in new starts in April of each policy period coincided with notable trends in 1-month prevalence results. Using our method of defining eligibility and nonuse, approximately one third of all LSA users (17-18 new starts per 1,000 recipients compared with 60 prevalent fills per 1,000 recipients) were new starters in the peak use month of April (Figure 3). During the month of July, an off-season in NC, only one sixth

FIGURE 3 *Incident LSA Starts: Monthly LSA Starts per 1,000 Nonusers*



** New starters were nonusers of LSA products for the 12-month period immediately preceeding LSA use (1-year run-in) for each monthly rate.*
LSA=low-sedating antihistamine; OTC=over the counter; Rx=prescription.

TABLE 3 *LSA Market Shares and Subsequent Share Changes Following OTC Conversion of Loratadine and the State Medicaid OTC Coverage Policy Change*

	Referent (Baseline) Feb.-Jun. 2002	OTC Noncoverage Feb.-Jun. 2003		OTC Coverage Feb.-Jun. 2004	
LSA	Market Share No. of Claims (%)	Market Share No. of Claims (%)	Absolute Change (%)	Market Share No. of Claims (%)	Absolute Change (%)
Loratadine	92,906 (38.1)	24,447 (9.3)	-28.8	11,453 (4.1)	-5.2
Cetirizine	85,431 (35.0)	127,157 (48.5)	13.4	141,232 (51.1)	2.7
Desloratadine	12,626 (5.2)	34,124 (13.0)	7.8	35,427 (12.8)	-0.2
Fexofenadine	52,894 (21.7)	76,698 (29.2)	7.5	88,217 (31.9)	2.7
Total	243,857 (100)	262,426 (100)		276,329 (100)	

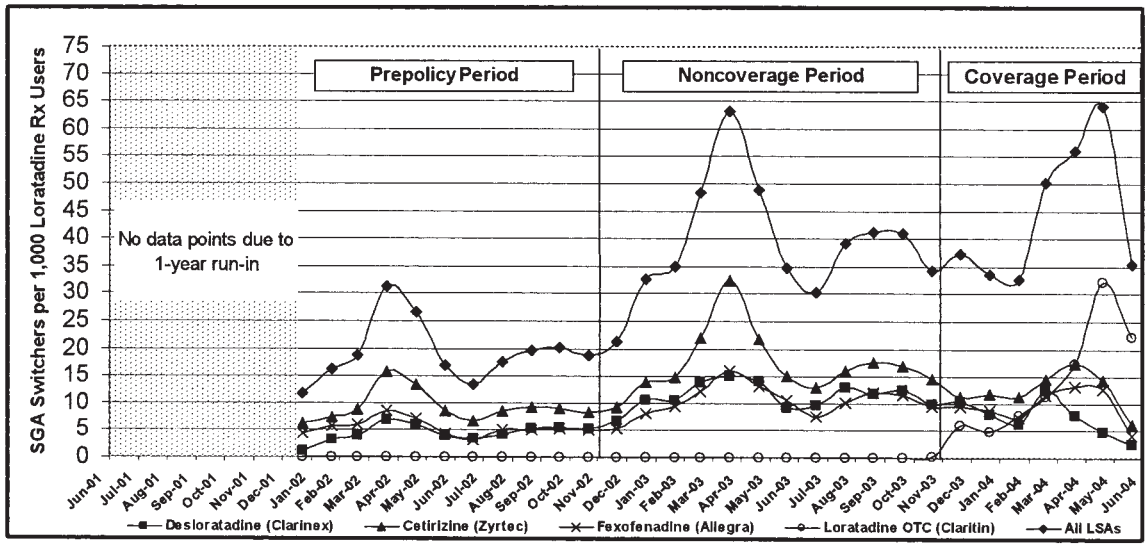
LSA=low-sedating antihistamine; OTC=over the counter; Rx=prescription.

of all LSA use was the result of new LSA starts (7 new starts per 1,000 recipients versus 41-43 fills per 1,000 recipients). The difference in ratios is seasonal and likely reflects the addition of seasonal LSA starters to a baseline rate of perennial starters.

In assessing the users who had switched from loratadine Rx to other products, we observed 3 distinct results in the 3 periods of interest (i.e., referent-baseline, OTC noncoverage, and OTC coverage). The baseline rate of switching from Rx loratadine to another LSA ranged from 10 per 1,000 recipients in the low-use months to a peak of 31 per 1,000 in the month of April (Figure 4). In contrast, during the OTC noncoverage period, switching from loratadine Rx ranged from 30 to 35 per 1,000 recipients in the low-use months to a peak of 63 per 1,000 in the month of April. For the months with comparable data (January-November), the difference in the area under the curve amounted to a difference of 237 switches per 1,000 recipients, or a 112% increase from a baseline of 212 to 449 switches per 1,000 recipients over that period. These time-series results in conjunction with rate-ratio results suggest that there was very little out-of-pocket loratadine OTC use (shown later) and that the 112% increase in switching, representing 8,380 switchers, was the result of noncoverage of loratadine OTC.

A small increase above seasonal trends in switching to loratadine OTC was found in May 2004 during the loratadine OTC coverage period. This spike coincides with the rollout of a pharmacist-based OTC initiative put forth by the NC Medicaid

FIGURE 4 Incident Switching: LSA Switchers per 1,000 Loratadine Rx Users



** Exclusive use of loratadine was required for the 12-month period immediately preceding LSA use (1-year run-in) for each monthly rate.*
LSA=low-sedating antihistamine; OTC=over the counter; Rx=prescription.

Drug Utilization Review Board. Despite the resultant increase in switching to loratadine OTC, loratadine Rx users were much less prevalent in the month immediately preceding the initiation of OTC coverage (n = 734) versus the month immediately preceding initiation of OTC availability (n = 13,773), meaning that there were fewer existing loratadine Rx users to switch to the much cheaper OTC product when coverage was initiated (approximately 1 user during coverage for every 20 during noncoverage).

Recipients in the OTC noncoverage interval were 2.16 (95% CI, 2.10-2.22) times more likely to switch from loratadine Rx to a different Rx LSA than recipients in the referent-baseline period using the rate-ratio method (Table 2). Using the same ratio construction, recipients were only slightly more likely to discontinue use in the noncoverage period than in the coverage period (rate ratio, 1.11 [95% CI, 1.09-1.13]). This suggests that very few recipients either self-purchased loratadine OTC after it became available or discontinued LSA use as a result of the policy change. An examination of the other LSAs on the market showed that the largest gain in market share was observed for cetirizine (13.4%, Table 3) although desloratadine had the largest rate of switching from loratadine Rx (rate ratio, 3.1 [95% CI, 2.91-3.3]), with a market share increase of 7.8% (Table 3). This suggests that new LSA users were most likely to initiate therapy with cetirizine, while existing loratadine users were most likely to switch to desloratadine. The reverse outcome occurred in the OTC coverage interval during which switch rates to loratadine OTC were consistently lower. Recipients were only 0.34 (95% CI, 0.32-0.37) times as likely to switch to loratadine OTC from another Rx LSA during the OTC coverage period as they were to switch to loratadine Rx in the referent-baseline period (Table 4). Additionally, the rate of starting loratadine OTC was only 0.18 (95% CI, 0.17-0.18) times that of loratadine Rx in the referent period.

Discussion

Medicaid OTC coverage continues to vary significantly by state. At least 1 OTC drug other than insulin was covered by all states with the exception of Louisiana in 2004.[21] Most OTC drugs are covered in Delaware, Minnesota, Nevada, New Hampshire, New Mexico, Oregon, Texas, Virginia, and Wyoming.[21] Many OTC drugs (e.g., histamine-2 antagonists, allergy drugs, analgesics) are covered in states like California, Indiana, Nebraska, South Carolina, and Vermont although restrictions and/or limitations were placed on certain drugs.[21] Other states, including NC, cover only a few select OTC drugs (e.g., loratadine and omeprazole).[21] Of relevance to this study, coverage decisions for OTC products are typically made coincident with OTC approvals from the FDA. A delay in extending coverage to the new OTC availability may lead to increased product switching to alternative covered products.

Following OTC conversion of loratadine, most NC Medicaid recipients seem to have switched from loratadine Rx to an alternative covered Rx (Medicaid-covered) product. Although all other LSAs accounted for some portion of loratadine Rx's loss of market share, the largest rate of switching was

TABLE 4 Rate Ratios for the Comparison of the OTC Coverage Period With the Referent (Baseline) Period

		Period			
		Referent (Baseline) Jul.-Nov. 2001 → Feb.-Jun. 2002	OTC Coverage Jul.-Nov. 2003 → Feb.-Jun. 2004		
Switch from	Switch to*	Rate/1,000†	Rate/1,000†	Rate Ratio	95% CI for Rate Ratio
No LSA	Loratadine (Rx/OTC)	23	4	0.18‡	0.17-0.18
Another LSA§	Loratadine (Rx/OTC)	44	15	0.34‡	0.32-0.37
Cetirizine	Loratadine (Rx/OTC)	48	12	0.25‡	0.23-0.28
Desloratadine	Loratadine (Rx/OTC)	–‖	25	–‖	–‖
Fexofenadine	Loratadine (Rx/OTC)	38	17	0.44‡	0.39-0.49

** Switches to Rx or loratadine OTC are dependent on the period; in the referent period, the switch is to loratadine Rx while in the OTC coverage period, the switch is to loratadine OTC.*

† Rate/1,000 is defined as the number of switchers per 1,000 eligible users. For this table, LSA users had to appear in both the 5-month preinterval of the referent period (Jul.-Nov. 2001) and the 5-month preinterval of the noncoverage period (Jul.-Nov. 2003). In the preinterval of the referent period, there were 1,020,856 nonusers of LSAs, 16,563 users of fexofenadine, and 28,317 users of cetirizine. In the preinterval of the OTC coverage period, there were 1,150,548 nonusers of LSAs, 30,570 users of fexofenadine, and 57,270 users of cetirizine.

‡ P <0.001 for chi-square test of the null hypothesis that the rate of switching in the referent period was the same as the rate of switching in the OTC coverage period.

§ Another LSA refers to the combination of switches from the covered drugs: cetirizine, desloratadine, or fexofenadine.

‖ Desloratadine was not available during the referent period; therefore it was not possible to calculate a rate ratio for this switch.

CI=confidence interval; LSA=low-sedating antihistamine; OTC=over the counter; Rx=prescription.

observed for desloratadine (loratadine Rx → desloratadine). The switch rate for desloratadine was more than 3 times greater following OTC conversion. This result is not surprising since desloratadine is the principal active entity of loratadine. Even so, the rate of switching from loratadine Rx to cetirizine and from loratadine Rx to fexofenadine was nearly twice as great after the OTC conversion of loratadine compared with the rates prior to OTC conversion. While this result seems inherently obvious given the noncoverage of loratadine OTC, it is the magnitude of switching and attribution of the policy effect above and beyond baseline switch rates that is germane to the analysis.

Unlike the effect observed in the noncoverage period, product switching following coverage of loratadine OTC a year later lagged behind that of the referent-baseline period. In comparison with baseline switch rates, our results indicate that there was relatively little switching to loratadine OTC from another (Rx) LSA product. This could indicate that once they have switched to an alternative product, physicians and patients were hesitant to switch back or initiate the use of an OTC product despite an economic incentive (i.e., $2 lower copay [$1 versus $3] per loratadine pharmacy claim). One explanation may be that the economic incentive was not large enough in the NC Medicaid population. In a privately insured population, a $10 differential in recipient out-of-pocket cost has been shown to influence utilization.[22]

Our data support the intuitive hypothesis that Medicaid programs will realize more use of the Rx-to-OTC conversion if OTC coverage is coincident with OTC availability rather than delayed. This conclusion is supported by the relative success in converting persons to loratadine OTC who previously used loratadine Rx as a result of the grace period associated with the legacy stock provision (Figure 4).

In fact, switches to loratadine OTC outpaced all other LSAs in May and June 2004 for existing users of loratadine Rx. In the month immediately preceding the federal policy change (Rx-to-OTC conversion of loratadine) in November 2002, there were 13,773 enrollees with loratadine claims. By the time the state policy change occurred (OTC coverage) in November 2003, there were only 743 enrollees with loratadine claims. While not all of the 13,773 prepolicy users would have remained on loratadine after the Rx-to-OTC conversion, our results suggest that most would have transitioned to the Medicaid-covered OTC product.

Various approaches have been employed by researchers to evaluate OTC switching behavior.[7-10,15] However, we are unaware of previous literature that has been able to measure or approximate OTC use empirically using administrative claims data. In large part, this is because OTC use is difficult to track in the absence of administrative claims data. Using the trend and market-share analysis of pharmacy claims alone, researchers would tend to overestimate the relationship between policy changes and switching to alternative, covered products because of the loss of OTC claims in the denominator. In this study, we utilized an alternative method of quantifying switching behavior in the absence of administrative claims for loratadine OTC.

Discontinuation of paid claims (a proxy for combined

discontinuation and OTC use) remained steady over time, thus suggesting very minimal, if any, loratadine OTC use during the noncoverage period (rate ratio, 1.11). The additional 11% increase in discontinuation from the referent-baseline period to the noncoverage period may be the result of either (1) loratadine OTC use or (2) LSA discontinuation altogether. It is impossible to determine from pharmacy claims which of these outcomes was more common. The use of a patient survey would be necessary to determine out-of-pocket OTC use.

The minimal change in discontinuation rates over time in combination with time-series results suggests an additional 8,380 switchers above baseline rates and permits an estimate of lost cost savings. The policy effect can be translated into monetary terms by multiplying the cost difference between the average paid claim amounts for Rx-only LSAs in the coverage period ($58.64 in Table 1) and loratadine OTC claims ($20.43 in Table 1) by the number of switchers attributed to noncoverage (8,380). The resulting first-fill opportunity cost associated with noncoverage would be $320,200. Given a monthly average of 53,281 LSA users during the OTC coverage period (Table 1), this translates to an opportunity cost of $6.01 per LSA pharmacy claim that is directly attributable to not covering the OTC product at the time of conversion (federal policy change). Though the average cost per LSA pharmacy claim dropped $4.15 (-6.6%) from $62.79 in the baseline period to $58.64 in the OTC coverage period, the time-series and rate-ratio results above suggest that an additional $6.01 (-10.2%) could have been saved per LSA claim had OTC coverage been in effect at the time of the conversion of loratadine to OTC status. Of course, this extrapolation is based on many assumptions, and this study was not designed as a cost study to account for nondrug costs such as physician office visits or other variables involved in calculating total health care and indirect costs. However, these nondrug factors are more likely to increase this opportunity cost (lost savings).

Cetirizine was the most common choice for new LSA starts (Figure 3), while desloratadine was the most common LSA switch as a result of the policy change (Table 2). Drawing conclusions from the time-series results alone, one may infer that cetirizine was the dominant choice for switchers. This conclusion would be erroneous, however, since baseline switching to cetirizine (66/1,000 loratadine Rx users [Table 2]) was already pronounced prior to OTC conversion of loratadine, while desloratadine lagged (30/1,000 loratadine Rx users [Table 2]). The rate-ratio approach accounted for baseline switching, thus accounting for prepolicy market conditions so that a direct attribution of effect could be given to the policy change in question.

Limitations

Foremost among the limitations of this study is the relatively large number of Medicaid recipients who continued to incur claims for loratadine Rx through the noncoverage period. This is the result of a Medicaid legacy stock (grace period) provision that is part of the federal Medicaid rebate program whereby pharmacies can continue to bill (and receive payment) for the Rx-only product until the stock is depleted. These claims are for NDC numbers representing previously Rx-only products whereas loratadine OTC claims were new NDC numbers for the newly marketed brand and generic OTC products. This is an important destinction, given the cost differential for reimbursement ($88.88 for the Rx NDC vs. $20.43 for the OTC NDC [Table 1]). The legacy stock provision may have reduced the immediate impact of the noncoverage effect in time series, though most pharmacies did not have legacy stock for more than a few months. This limitation may make the time-series results less generalizable to private-payment pharmacy benefit plans that may have NDC blocks for OTC-equivalent drugs. However, this limitation is reduced in importance because the majority of pharmacies did not have legacy stock remaining at 7 months post-OTC conversion (November 27, 2002-June 30, 2003); therefore, nearly all switching behavior was captured using the second quantifiable approach. In fact, another value of the rate-ratio method used in the present study was the ability to capture longitudinal switching behavior.

Second, factors uncommon to both policy and referent-baseline periods may have confounded the results. When constructing rate ratios, the researcher must ensure that participants differ only in exposure.[23] Any factor, other than the policy itself that exists in the policy period and not in the referent period or vice versa may lead to spurious results. Certainly, the latter half of 2002 and all of 2003 and 2004 were marked by heavy promotion of both desloratadine Rx and loratadine OTC. It is not clear what role these or other factors played in the interpretation of the results found in the present study.

We also did not assess the use of therapeutic alternatives to LSAs in allergic rhinitis, including nasal steroids or montelukast (Singulair), which was approved by the FDA for the additional indication of allergic rhinitis on December 31, 2002.[3] Lakomski and Chitre estimated that as much as 25% of the use of montelukast was for allergic rhinitis in the 12-month period ended August 31, 2002, long before the FDA approval for this indication.[24]

We were also not able to calculate a rate ratio for switching from desloratadine to loratadine OTC because of the timing of the FDA approval of desloratadine. The likely effect was to diminish the rate ratio for the sum total of switching from other LSAs to loratadine OTC. Visual inspection of the rates (not rate ratios) found in the OTC coverage period (switching from desloratadine to loratadine OTC was found to occur at a rate of 25 enrollees per 1,000 desloratadine users [Table 4], outpacing all other drug class members) suggests that the effect of this limitation may not be large. This result is consistent with the effect seen from the noncoverage period in which the most common switch was from loratadine to the nearly chemically identical desloratadine.

As an alternative to the rate-ratio method, we conducted a supplementary analysis of incident use in this Medicaid population over 3 years using an autoregressive integrated moving average (ARIMA) model.[17] We used an ARIMA (0,0,1) model with adjustment for 12-month seasonality. This model was used to forecast LSA use under varying policy scenarios. However, 2 major limitations arose from the ARIMA analysis. Since loratadine OTC was not a covered product during the period from November 2002 to November 2003, we cannot accurately capture nor assume OTC use or nonuse from administrative claims data using time series alone. Furthermore, we had less than the preferred 20 months of data to identify (overlay) our model (after adjusting for seasonality). Thus, this approach was determined to be inadequate for our study and probably for other studies of Rx-to-OTC conversions.

In our analysis, we chose to use eligibility criteria that maximized the inclusion of LSA pharmacy claims. Using the "any eligibility" criterion for all analyses with run-in periods enabled us to capture 80% to 90% of all LSA use. Had we used continuous eligibility criteria, we would have captured only 50% to 60% of all LSA use. We conducted a separate supplementary analysis that required continuous eligibility, and only small differences in rates (less than 2%) were observed when compared with the "any eligibility" models; thus, we present here the more inclusive analysis using the "any eligibility" criterion.

We also required exclusive use of drug products for all of the analyses in prepolicy periods. Requiring 1 year of exclusive use for incident switching in time series and the prepolicy period, exclusive use for the rate-ratio calculations was necessary to elicit a more true policy effect. Inclusion of recipients making multiple switches during the prepolicy periods might have led to misclassification errors. An infinite number of user classifications exists for these multiple switchers. Requiring exclusive use of a given LSA for a predefined period ensures appropriate classification for true users of specific drugs. Using an alternative criterion such as "drug of last fill" simplifies classification but would appear to increase the likelihood of misclassification of drug switches attributable to the policy change. Since the focus of the present study was on switching rates and not aggregate switching or aggregate costs, we chose the more conservative approach. We acknowledge that rates of switching due to the policy changes may be slightly different for these "multiple" switchers but that these actual rates would be quite difficult to determine, and these types of switchers were substantially less common.

We believe that our multifaceted approach is necessary when evaluating product switching for LSAs in a Medicaid program, as well as other populations, especially when considering drugs that are used as needed. The rate-ratio approach should perform even more robustly with medications that are used for chronic conditions where continuous use affords more precise measures and reduces the likelihood of misclassification resulting from the exclusion of subjects with use of multiple products in a therapeutic class. We also believe that the rate-ratio approach described herein has useful application to analyses of multiple insurance plans over a single period, using one of these plans as a referent.

The policy change made in November 2003 to cover loratadine OTC was the first such OTC coverage for other than insulin products in the NC Medicaid program. The dissemination of OTC coverage information to prescribers and pharmacists as well as the learning curve associated with claims adjudication for nonlegend drugs likely contributed to the slow uptake of loratadine OTC. It is likely that there will be additional benefits from this policy change to cover loratadine OTC, both for additional loratadine OTC claims as well as future OTC products. The NC Medicaid program is now better positioned for future LSA conversions, as well as potential class conversions such as the possible introduction of OTC statin drugs.[13]

Conclusion

Medicaid recipients switched to another covered Rx-only LSA in the loratadine noncoverage period at a rate greater than twice that of the baseline period of coverage (2.16 [95% CI, 2.10-2.22]). After a subsequent policy change to extend coverage to loratadine OTC, there was minimal switching to loratadine OTC from another Rx LSA despite a copayment differential of $2 ($3 for an Rx LSA versus $1 for loratadine OTC). Though the average cost per LSA pharmacy claim dropped $4.15 (6.6%), from $62.79 in the baseline period to $58.64 in the OTC coverage period, time-series and rate-ratio results suggest that an additional $6.01 (10.2%) could have been saved per LSA pharmacy claim had OTC coverage been in effect at the time of the conversion of loratadine to OTC status. Though OTC conversion and subsequent OTC coverage both seem to have reduced overall LSA expenditures, failure to cover the OTC product at the time of OTC conversion resulted in substantial opportunity costs in lost savings. Medicaid programs, as well as perhaps private plans, may capture these savings and prevent accelerated switching at the time of OTC conversion by making coverage decisions before FDA approval of conversion of drugs from Rx to OTC status.

ACKNOWLEDGMENTS

The authors would like to thank Emily Brouwer, MPH, PharmD candidate, University of North Carolina School of Pharmacy, Chapel Hill, and the *JMCP* peer reviewers and editor-in-chief for their constructive advice with this manuscript.

DISCLOSURES

Funding for this research was provided by the Pharmacy Foundation of North Carolina, the University of North Carolina School of Pharmacy, and AccessCare of North Carolina (a nonprofit organization) and was obtained by authors Troy K. Trygstad, Richard A. Hansen, and Steven E. Wegner.

The authors disclose no potential bias or conflict of interest relating to this article. Trygstad served as principal author of the study. Study concept and design were contributed primarily by Trygstad and Hansen, with input from Wegner. Data collection was primarily the work of Trygstad, with input from Wegner; data interpretation was the work of Trygstad and Hansen. Drafting of the manuscript was the work of all authors; its revision was the work of Trygstad.

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