

Cost-Motivated Treatment Changes in Commercial Claims:

**Implications for Non-
Medical Switching**

August 2017

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Health benefits designs in both private and public health insurance programs include mechanisms to control the costs of care, resulting in many health care choices being made with a focus on financial concerns that could outweigh clinical factors. This can particularly be true for interventions involving prescription drugs and biologics. In some cases, choice of prescription therapy may be driven by patient cost sharing and affordability controls. In others, plan benefit design may result in “non-medical switching” between prescription therapies. Whether by conscious design or inadvertent result, patients with significant chronic disease whose condition has been stabilized on a particular drug regimen can lose access to continued coverage for their therapy, forcing physicians to switch the patient’s prescription to an alternative drug.

Whatever the mechanism by which non-medical switching is induced, it raises significant clinical issues for patients who find themselves being switched from a therapy known to be working toward a therapy of presently unknown efficacy. The immediate consequence of cost-motivated treatment changes is the potential for treatment failure. In the intermediate and longer term, the consequences of remediating that treatment failure may be substantial, potentially off-setting some or all of the immediate “savings” that accrue because of the switch in therapies.

In a prior study for the Institute for Patient Access (IfPA), The Moran Company investigated whether the effect of non-medical switching on Medicare spending could be demonstrated by analyses of Medicare claims data. In that study, we found that switching between Part B drugs occurred at different levels in patients being treated for various conditions. We further found that for rheumatoid arthritis patients, total non-drug Medicare Part B spending increased materially for patients with one or more switches to less expensive medications.¹

IfPA asked us to extend our prior analysis of switching issues in Medicare by examining these issues in commercial claims data. Using a sample of Truven’s MarketScan® Commercial Claims and Encounters and Medicare Supplemental database for chronic conditions of interest, we analyzed the prevalence of switching for various populations and examined the drug and non-drug costs of studied patient populations before and after identified switching events. Since it is not possible to track patients across plans, our claims come from patients who maintained consistent coverage for at least three of the five years in claims data. Thus, our analysis probably understates the level of switching in the populations being studied.

As we present in the paper that follows, we again found evidence to support our hypothesis that cost-motivated treatment changes can lead to higher costs for patients with various conditions, in this case for patients with Crohn’s disease, osteoarthritis, multiple sclerosis, rheumatoid arthritis, and psoriasis.

¹ *Cost-Motivated Treatment Changes in Medicare Part B: Implications for Non-Medical Switching*. The Moran Company (September 2016). <http://1yh21u3cjptv3xjder1dco9mx5s.wpengine.netdna-cdn.com/wp-content/uploads/2016/10/Switching-Study-Report-FINAL.pdf>

Highlights of Our Findings:

Overall

- Our analysis of commercial claims found that the different diagnostic cohorts had rates from 5% to 64% for switching between chronic medications for the twelve conditions selected for analysis.
- In comparison to prior examination of Medicare claims analysis, this work is able to examine both physician office and pharmacy claims.
- In comparison to that prior work, we can see switching behavior resulting in spending differentials across a broader arrays of conditions.
 - In our prior work, we found that material differences in non-drug medical spending after a switch occurred only for patients with rheumatoid arthritis.
 - In the present analysis we reached this finding for five conditions; for two conditions, our finding was statistically significant.
- It is important to note that population differences between the Medicare and commercial populations make direct comparisons more complex than we can capture in this analysis.
- Limitations in claims data regarding clinical motives for switching behavior also affect the interpretation of our results.
- Notwithstanding these limitations, in this analysis, we found five conditions for which we have direct evidence that patients switched to lower-cost drugs subsequently experience, on average, higher covered non-drug costs downstream of the switch: Crohn's disease, multiple sclerosis, chronic obstructive pulmonary disorder, psoriasis, and rheumatoid arthritis.
- For these conditions, we also see higher post-switch non-drug costs for those who experienced multiple switches.
- For six of the remaining seven conditions, we found that patients who switched to a lower cost medication did not have significantly different non-pharmacy spending compared to those that switched to a higher cost medication.
 - Only chronic pain patients who switched to a lower cost medication were found to have significantly lower non-pharmacy spending than those who switched to a higher cost medication.
- As found in the prior work, patients who switched medications were likely (>50%) to switch again in eight of the twelve disease states.
- Across all the conditions with adequate statistical power, patients who did not switch drugs had the lowest spending, and spending growth, observed in our sample compared to patients with one or more switches of any type.
- Because our data were designed to track patients with continuous coverage, our results do not include individuals who switch plans and are required to go through step therapy again as a result.
 - Consequently, our findings probably understate the level of switching for patients covered by commercial plans.

Disease Specific

- As a result of the differences between the two study populations, it is not surprising that the prevalence of switching in various patient populations differs in the two analyses:
 - Rheumatoid Arthritis – the switching rate for Medicare beneficiaries was 9.9%, but within the commercial data 23.0% of patients were observed to have switched.
 - Crohn’s Disease – the switching rate for Medicare beneficiaries was 8.1%, but within the commercial data 38.3% of patients were observed to have switched.
 - Immunodeficiency – Switching for Medicare beneficiaries was 29.4%, whereas only 10.0% of commercial patients were observed to have switched.
- Crohn’s Disease –
 - Patients who did not switch appeared the most stable, as they had the lowest spending and spending growth levels observed for Crohn’s patients in our sample.
 - Patients who switched to a lower cost medication had a similar increase in spending to those patients with multiple switches.
 - Patients who switched to a higher cost medication had a significantly lower difference in per member per month (PMPM) spending during the periods of our analysis.
- Multiple Sclerosis –
 - The group of patients who switched to a lower cost medication had the largest increase in PMPM spending compared to the other three groups.
 - Patients who switched to a higher cost medication had a significantly lower change in PMPM spending compared to those that switched to a high cost medication.
- For patients with psoriasis, chronic obstructive pulmonary disorder (COPD) and rheumatoid arthritis, we reached similar findings: –
 - Patients who switched to a lower cost medication had a similar change in PMPM spending than those with multiple switches.

The balance of this report discusses the results of each diagnostic cohort in detail and follows with a discussion of methodology. Appendices provide additional background.

Results

In the present analysis, we have adopted a number of assumptions that are similar to those used in our Medicare study. For example, we have assumed that a patient switching from a lower cost drug to a higher cost drug would not do so for cost motivated reasons. Therefore, we presume that such a switch would not be considered a non-medical switch for purposes of this analysis. In the section that follows, we present information about prevalence of switching by patient population and note changes observed in per member per month (PMPM) spending across patients with various kinds of identified switches.

In our analysis, we defined the first date a patient appeared with an applicable diagnosis as the “index date.” Patients were required to be eligible for pharmacy and medical benefits from six months prior to the index date, defined as the “prior period”, to twelve months after the index date, defined as the “post period”. Our spending comparisons presented below measure spending for patients in these periods based on the switches observed for those patients.

Switching

As can be seen in Table 1 (below), switching behavior varied across the various diagnostic cohorts for the twelve conditions selected for initial analysis. Switching ranged from 64% of patients (Asthma) to only 5% (Hypercholesterolemia). Additionally, if one switch was made, patients were likely to switch again in all but four conditions. For example, the cohort of hypercholesterolemia patients only had 5% of patients with switching; however, 66% of patients with switches switched again. The percent of patients that switched again ranged from 27% to 83% across all diagnoses.

Table 1 – Summary of Switching Behavior Across Diagnostic Cohorts

Diagnoses	Total Number of Patients	Total Switches	Number of Patients who Switched One or More Times	Number of Patients who Switched 2+ Times	Percentage of Patients with at least one Switch	Percentage of Patients who Switched Again
Asthma	83,161	191,298	14,455	38,798	64%	73%
Crohn's Disease	23,047	28,518	3,092	5,736	38%	65%
Chronic Pain	82,185	72,787	6,377	13,886	25%	69%
COPD	269,627	78,486	18,075	17,557	13%	49%
Cystic Fibrosis	753	794	29	142	23%	83%
Hepatitis C	2,097	2,210	121	517	30%	81%
Hypercholesterolemia	76,126	13,117	1,280	2,525	5%	66%
Immunodeficiency	2,790	426	202	76	10%	27%
Multiple Sclerosis	14,864	7,112	1,662	1,843	24%	53%
Osteoporosis	13,605	1,652	364	371	5%	50%
Psoriasis	31,215	3,848	1,527	786	7%	34%
Rheumatoid Arthritis	43,249	19,303	6,197	3,754	23%	38%

Crohn's Disease

Nearly 40% of the Crohn's disease patients demonstrated switching behavior during the post period. Patients that did not switch medications had the lowest PMPM spending in the post period as well as the smallest change from prior-to-post period. For those patients that switched only once, essentially half of them switched to a higher cost medication. Those patients that switched to a higher cost medication had significantly lower change in their PMPM spending ($t = 4.71, p < .0001$) than those that switched to a lower cost medication.

These results support a finding that for patients with Crohn's disease, cost-motivated treatment changes may have resulted in higher levels of medical spending.

Table 2 – Crohn’s Disease - Switching Frequency and Cost Implications

Switch Category	No Switches		1 Switch				>1 Switches	
			Switched to Lower		Switched to Higher			
	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD
Number of Patients	14,219	62%	1,441	6%	1,651	7%	5,736	25%
Non-Pharmacy PMPM Spending								
Prior Period	\$ 1,314	\$ 3,520	\$ 1,384	\$ 3,379	\$ 1,423	\$ 3,520	\$ 1,726	\$ 3,854
Post Period	\$ 3,386	\$ 6,596	\$ 5,883	\$ 9,290	\$ 4,578	\$ 8,093	\$ 6,615	\$ 9,874
Difference Between Periods	\$ 2,072	\$ 3,076	\$ 4,499	\$ 5,910	\$ 3,155	\$ 4,573	\$ 4,890	\$ 6,020

Multiple Sclerosis

Switching behavior was less prevalent in MS, as only 24% of patients qualified as switching in the post-index period. The frequency of people who switched to a higher cost medication was nearly double those who switched to a lower cost medication. As seen in Crohn’s disease, those patients who switched to a higher cost medication also had a significantly smaller PMPM change from prior-to-post period compared to those who switched to a lower cost medication ($t = 4.88$, $p < .0001$). Interestingly, those patients that had only one switch to a lower cost medication saw the highest change in PMPM across the four mutually exclusive groups.

Table 3 – Multiple Sclerosis - Switching Frequency and Cost Implications

Switch Category	No Switches		1 Switch				>1 Switches	
			Switched to Lower		Switched to Higher			
	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD
Number of Patients	11,359	76%	574	4%	1,088	7%	1,843	12%
Non-Pharmacy PMPM Spending								
Prior Period	\$ 1,057	\$ 3,107	\$ 1,269	\$ 2,648	\$ 1,044	\$ 2,072	\$ 1,143	\$ 2,570
Post Period	\$ 2,823	\$ 6,157	\$ 5,631	\$ 8,502	\$ 3,524	\$ 6,812	\$ 3,768	\$ 6,661
Difference Between Periods	\$ 1,766	\$ 3,050	\$ 4,362	\$ 5,855	\$ 2,479	\$ 4,740	\$ 2,625	\$ 4,091

Thus, our analysis tends to support the hypothesis that MS patients subject to non-medical switching have higher non-drug medical spending than patients who do not switch medications or switch to a higher cost prescription.

Psoriasis

Switching behavior was rare within the psoriasis cohort, as only 7% of patients switched medications. The patients that had one switch and switched to a lower cost medication had a PMPM change that was similar to patients that did not switch medications. Also, patients with multiple switches saw a similar change in PMPM costs as those who switched once but went to a higher medication. Unlike the previously mentioned cohorts, the change in PMPM was not significantly lower for patients that switched to a lower costing medication ($t = 1.11, p = .27$).

Table 4 – Psoriasis - Switching Frequency and Cost Implications

Switch Category	No Switches		1 Switch				>1 Switches	
	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD
Number of Patients	28,902	93%	719	2%	808	3%	786	3%
Non-Pharmacy PMPM Spending								
Prior Period	\$ 398	\$ 1,233	\$ 449	\$ 1,331	\$ 425	\$ 1,340	\$ 419	\$ 1,070
Post Period	\$ 986	\$ 2,200	\$ 1,097	\$ 2,068	\$ 956	\$ 1,928	\$ 1,090	\$ 2,173
Difference Between Periods	\$ 588	\$ 967	\$ 648	\$ 737	\$ 531	\$ 588	\$ 671	\$ 1,103

Chronic Obstructive Pulmonary Disorder (COPD)

Thirteen percent of COPD patients switched medications during the post period. Patients who did not switch were clearly the least expensive sub-group of the cohort and also saw the smallest change in PMPM from prior-to-post period. When only one switch occurred, patients were nearly twice more likely to switch to a more expensive medication. While patients who switched to a more expensive medication did have a smaller change in PMPM (\$2,192 vs. \$2,316), the difference between the groups was not significant ($t = 1.25, p = .21$). Patients with multiple switches were the most expensive and had the most dramatic increase from prior-to-post period.

Table 5 – Chronic Obstructive Pulmonary Disorder - Switching Frequency and Cost Implications

Switch Category	No Switches		1 Switch				>1 Switches	
			Switched to Lower		Switched to Higher			
	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD
Number of Patients	233,995	87%	6,569	2%	11,506	4%	17,557	7%
Non-Pharmacy PMPM Spending								
Prior Period	\$ 755	\$ 2,365	\$ 1,159	\$ 3,026	\$ 964	\$ 2,708	\$ 1,298	\$ 3,334
Post Period	\$ 2,062	\$ 5,065	\$ 3,475	\$ 7,070	\$ 3,156	\$ 6,164	\$ 4,469	\$ 8,035
Difference Between Periods	\$ 1,307	\$ 2,700	\$ 2,316	\$ 4,044	\$ 2,192	\$ 3,456	\$ 3,171	\$ 4,701

Rheumatoid Arthritis (RA)

23% of the patients in our RA sample switched medications during the post period. As seen in other cohorts, the patients who did not switch medications had the smallest non-pharmacy PMPM of the four groups. The majority of patients with one medication switch went to a more expensive drug. Additionally, those patients that switched to a more expensive drug also had a smaller PMPM change from prior-to-post period compared to patients that switched to a lower cost medication. However, the difference between these two groups was not significant ($t = 0.94, p = .35$).

Table 6 – RA - Switching Frequency and Cost Implications

Switch Category	No Switches		1 Switch				>1 Switches	
			Switched to Lower		Switched to Higher			
	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD
Number of Patients	33,298	77%	702	2%	5,495	13%	3,754	9%
Non-Pharmacy PMPM Spending								
Prior Period	\$ 967	\$ 2,362	\$ 1,316	\$ 2,802	\$ 905	\$ 1,901	\$ 1,016	\$ 2,344
Post Period	\$ 2,441	\$ 5,209	\$ 3,210	\$ 4,617	\$ 2,622	\$ 4,959	\$ 2,730	\$ 4,858
Difference Between Periods	\$ 1,474	\$ 2,847	\$ 1,894	\$ 1,815	\$ 1,717	\$ 3,059	\$ 1,714	\$ 2,514

Other Diagnostic Conditions Analyzed

In addition to the above mentioned conditions (as reported in Tables 2-6), the results from seven other conditions fell into three categories.

Three of the conditions (asthma, osteoporosis, and hypercholesterolemia) had non-significant differences in non-pharmacy spending between those patients who switched from a low cost medication compared to those that switched to a high cost medication. Even when comparing total health care costs (i.e. both pharmacy and non-pharmacy spending combined), the patients that switched to a lower cost medication did not have significantly less spending than those that switched to a high cost.

Three of the conditions (cystic fibrosis, hepatitis C, and immunodeficiency) had either a small initial sample size or small switching rate that prohibits conclusions with regard to the impact of switching behavior.

One condition, chronic pain, did have significantly lower change of PMPM non-pharmacy spending for those patients who switched to a lower medication ($t = -2.32, p = .021$).

All tables for these seven additional conditions can be found in Appendix A.

PMPM Regardless of Switching Category

In Table 7 (see below), we examined average pharmacy and non-pharmacy (i.e. all medical expenses after excluding pharmacy) PMPM spending for all patients within the diagnostic cohorts. The pre-period is the six months prior to their first diagnoses, and we can see that every cohort across the board saw increased spending for both pharmacy and non-pharmacy in the post-period.

Table 7 – PMPM – Regardless of Switching Category

Diagnoses	Non Pharmacy Payments		Pharmacy Payments	
	Pre Period	Post Period	Pre Period	Post Period
Asthma	\$ 875	\$ 2,075	\$ 144	\$ 354
Crohn's Disease	\$ 1,428	\$ 4,431	\$ 190	\$ 750
Chronic Pain	\$ 2,616	\$ 5,949	\$ 246	\$ 583
COPD	\$ 809	\$ 2,300	\$ 115	\$ 297
Cystic Fibrosis	\$ 3,919	\$ 10,366	\$ 507	\$ 2,233
Hepatitis C	\$ 1,107	\$ 3,433	\$ 321	\$ 5,914
Hypercholesterolemia	\$ 1,023	\$ 2,866	\$ 169	\$ 401
Immunodeficiency	\$ 12,436	\$ 18,737	\$ 467	\$ 1,431
Multiple Sclerosis	\$ 1,075	\$ 3,100	\$ 510	\$ 2,459
Osteoporosis	\$ 1,158	\$ 2,647	\$ 238	\$ 596
Psoriasis	\$ 401	\$ 990	\$ 100	\$ 472
Rheumatoid Arthritis	\$ 969	\$ 2,501	\$ 211	\$ 838

Methodology

Commercial Claims Data

This retrospective cohort analysis used the Truven Health Marketscan® Commercial Claim and Encounters Database from 2011-2015. This extract used from the database contains information for 3.9 million people from 2011-2015. One limitation of studies with commercial claims data involves an inability to track patients that move from one plan to another. To mitigate this problem, the database we received was drawn from patients that had three years of continuous coverage during the study period. Detailed information within this database include inpatient and outpatient visits/services, outpatient prescription drug claims, enrollment information, and demographic variables. Survey participants in the commercial database are from self-insured employers as well as health plans of different types.

Demographic Information

Demographics for the various disorders can be found in the Appendix B. As expected, the average ages for all diagnoses cohorts were appreciably younger than what one would find in a Medicare analyses. Gender breakouts also appear to be similar to previously published reports. For example, RA, MS, and osteoporosis patients are largely female (68%, 75%, and 99%, respectively), while cystic fibrosis and hepatitis C patients are ~60% male (60% and 61%, respectively). Also, the patients in each cohort are not localized to one region of the country. For each diagnostic cohort, the southern region is most prevalent.

Identifying Participants

We created twelve analytic files, one for each disease under evaluation.² For each file, all patients with at least one diagnosis of interest³ in either an inpatient stay or any outpatient service from July 2011 to December 2014, were included in the sample frame of patients under study. The first date of the applicable diagnosis was then defined as the “index date.” Patients were required to be eligible for pharmacy and medical benefits from six months prior to the index date, defined as the “prior period”, to twelve months after the index date, defined as the “post period”. The post period includes the index date, and the prior period ends one day before the index date. If a patient appeared in multiple analytic datasets, they were included in each study. Patients were dropped from the study if they had Medicare coverage at any point during the evaluation period.

Identifying Applicable Medications

Within each disease state, the patient’s entire outpatient pharmaceutical data were extracted. All duplicate NDC codes within a patient were removed. We then examined the 100 most frequently

² Asthma, Crohn’s Disease, Chronic Pain, Chronic Obstructive Pulmonary Disease (COPD), Cystic Fibrosis, Hepatitis C, Hypercholesterolemia, Immunodeficiency, Multiple Sclerosis, Osteoporosis, Psoriasis, and Rheumatoid Arthritis.

³ Appendix C

occurring medications, by generic name. This list was assessed for medications that treat chronic symptoms of the respective disease state. In addition, IfPA also reviewed the list with assistance from clinical experts, adding a few medications that did not occur in the top 100 in our analysis. Finally, an internet-based review of chronic medications for each disease state was performed, which further refined the list of common medications. From this list, we then deleted all NDCs that were listed as being for short-term acute conditions.⁴ Once the list of medications was finalized, all NDC codes for the specified medications were pulled from the data. The final list of medications used for each diagnoses cohort can be found in Appendix D.

Standardized Monthly Cost of Pharmaceutical Treatment

Prescribed medications can come in various days' supply and prescribed regimens, so in order to create a standardized price for each medication to be used to evaluate switching behavior between drugs we calculated the cost per month for each drug. The pharmaceutical prices were standardized in one of two ways, depending on whether a days' supply field was available on the claim. For those medications found in the outpatient pharmaceutical table, the cost of the medication was divided by the days' supply and then multiplied by 30 (i.e. 30 days). For those medications found in the outpatient services table (i.e. infusions) where the concept of "days' supply" does not apply, we took the service date of the medication and then looked 30 days ahead. Any medications with the same generic name in the 30-day window then had payment information combined. Once all medications had total per month costs, the average cost across all patients were calculated.

We then defined patients into three switching strata depending on their switching behavior during the post-period. Patients were classified as 1) switching to pharmaceutical treatment with a standardized month cost of 20% more than the original drug, 2) switching to a drug with a standardized cost of at least 20% less than the original drug, or 3) not switching or switching to a drug that was within 20% in cost.

Total Per Member Per Month Medical Costs during the Prior and Post Periods.

To evaluate the total cost of treatment associated with switching, we summed all-cause treatment for inpatient, outpatient, and prescription services for the prior period and the post period for each patient. These total costs were then standardized to per member per month costs (PMPM) by dividing the total costs for all patients in each switching strata by either six (prior period) or 12 (post period).

Conclusion

The patients in our present analysis represent a materially different population than the Medicare population, which make direct comparisons between our two studies more complex than we can capture in this analysis. In contrast to our prior study, the current analysis is able to examine switching involving both physician-administered and pharmacy benefit drugs, but commercial claims data—as with Medicare—provide limited information about the motives for particular

⁴ The variable used was MAINTIN with a value of "3" ...short-term treatment of acute conditions".

switches. Notwithstanding these issues, we found five conditions for which we have direct evidence that patients switched to lower-cost drugs subsequently experienced, on average, higher covered non-drug costs downstream of those switches. In addition, we also found for another six conditions that switching to a lower cost medication did not result in less expensive non-pharmacy spending compared to those that did switch to a higher cost medication.

While it is possible to utilize this commercial claims database in order to evaluate switching, the results may underestimate the real-world effect of this behavior. Patients that change insurance carriers cannot be captured when the analysis requires continuous eligibility throughout the examination period. Individuals that changed carriers may be required to undergo step therapy again, which would increase switching rates.

Thus, as we found in our prior study of Medicare claims, our study of commercial claims supports the hypothesis that cost-motivated switching among treatments may lead to higher costs in patients with certain conditions.

Appendix A – Other Diagnostic Conditions Analyzed

Table A1 – Asthma - Switching Frequency and Cost Implications

Switch Category	No Switches		1 Switch				>1 Switches	
	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD
Number of Patients	29,908	36%	5,818	7%	8,637	10%	38,798	47%
Non-Pharmacy PMPM Spending								
Prior Period	\$ 755	\$ 2,061	\$ 874	\$ 2,323	\$ 722	\$ 1,789	\$ 1,001	\$ 2,329
Post Period	\$ 1,730	\$ 4,093	\$ 1,910	\$ 3,961	\$ 1,806	\$ 3,900	\$ 2,426	\$ 4,680
Difference Between Periods	\$ 975	\$ 2,032	\$ 1,035	\$ 1,638	\$ 1,084	\$ 2,111	\$ 1,425	\$ 2,351

Table A2 – Osteoporosis - Switching Frequency and Cost Implications

Switch Category	No Switches		1 Switch				>1 Switches	
	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD
Number of Patients	12,870	95%	178	1%	186	1%	371	3%
Non-Pharmacy PMPM Spending								
Prior Period	\$ 1,144	\$ 2,585	\$ 1,142	\$ 2,053	\$ 1,334	\$ 3,082	\$ 1,582	\$ 3,188
Post Period	\$ 2,611	\$ 4,886	\$ 3,139	\$ 5,942	\$ 3,715	\$ 6,547	\$ 3,123	\$ 4,951
Difference Between Periods	\$ 1,467	\$ 2,301	\$ 1,997	\$ 3,889	\$ 2,380	\$ 3,465	\$ 1,540	\$ 1,763

Table A3 – Chronic Pain - Switching Frequency and Cost Implications

Switch Category	No Switches		1 Switch				>1 Switches	
	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD
Number of Patients	61,922	75%	2,588	3%	3,789	5%	13,886	17%
Non-Pharmacy PMPM Spending								
Prior Period	\$ 2,248	\$ 5,712	\$ 3,620	\$ 8,637	\$ 3,439	\$ 7,688	\$ 3,850	\$ 8,482
Post Period	\$ 5,106	\$ 8,954	\$ 7,761	\$ 10,773	\$ 8,278	\$ 12,164	\$ 8,736	\$ 13,228
Difference Between Periods	\$ 2,859	\$ 3,242	\$ 4,141	\$ 2,136	\$ 4,839	\$ 4,476	\$ 4,886	\$ 4,746

Table A4 – Hypercholesterolemia - Switching Frequency and Cost Implications

Switch Category	No Switches		1 Switch				>1 Switches	
			Switched to Lower		Switched to Higher			
	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD
Number of Patients	72,321	95%	579	1%	701	1%	2,525	3%
Non-Pharmacy PMPM Spending								
Prior Period	\$ 1,018	\$ 2,786	\$ 1,148	\$ 2,820	\$ 1,316	\$ 3,564	\$ 1,062	\$ 2,756
Post Period	\$ 2,847	\$ 5,841	\$ 3,125	\$ 5,559	\$ 3,732	\$ 7,219	\$ 3,104	\$ 6,034
Difference Between Periods	\$ 1,829	\$ 3,055	\$ 1,977	\$ 2,740	\$ 2,416	\$ 3,655	\$ 2,042	\$ 3,279

Table A5 – Cystic Fibrosis - Switching Frequency and Cost Implications

Switch Category	No Switches		1 Switch				>1 Switches	
			Switched to Lower		Switched to Higher			
	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD
Number of Patients	582	77%	12	2%	17	2%	142	19%
Non-Pharmacy PMPM Spending								
Prior Period	\$ 4,285	\$ 12,234	\$ 10,547	\$ 19,169	\$ 293	\$ 432	\$ 2,293	\$ 8,835
Post Period	\$ 10,780	\$ 20,340	\$ 41,212	\$ 77,686	\$ 2,464	\$ 4,840	\$ 7,007	\$ 13,937
Difference Between Periods	\$ 6,496	\$ 8,106	\$ 30,665	\$ 58,517	\$ 2,170	\$ 4,408	\$ 4,714	\$ 5,102

Table A6 – Hepatitis C - Switching Frequency and Cost Implications

Switch Category	No Switches		1 Switch				>1 Switches	
			Switched to Lower		Switched to Higher			
	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD
Number of Patients	1,459	70%	23	1%	98	5%	517	25%
Non-Pharmacy PMPM Spending								
Prior Period	\$ 1,213	\$ 3,751	\$ 808	\$ 1,315	\$ 627	\$ 977	\$ 911	\$ 2,986
Post Period	\$ 3,547	\$ 7,625	\$ 2,918	\$ 4,044	\$ 2,825	\$ 4,738	\$ 3,248	\$ 6,106
Difference Between Periods	\$ 2,334	\$ 3,875	\$ 2,110	\$ 2,729	\$ 2,198	\$ 3,761	\$ 2,337	\$ 3,120

Table A7 – Immunodeficiency - Switching Frequency and Cost Implications

Switch Category	No Switches		1 Switch				>1 Switches	
			Switched to Lower		Switched to Higher			
	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD	n / mean	% / SD
Number of Patients	2,512	90%	100	4%	102	4%	76	3%
Non-Pharmacy PMPM Spending								
Prior Period	\$ 12,529	\$ 31,507	\$ 9,623	\$ 18,369	\$ 12,918	\$ 26,848	\$ 12,425	\$ 26,110
Post Period	\$ 18,490	\$ 29,792	\$ 18,262	\$ 21,644	\$ 21,008	\$ 24,029	\$ 24,468	\$ 35,884
Difference Between Periods	\$ 5,961	\$ (1,716)	\$ 8,639	\$ 3,275	\$ 8,090	\$ (2,819)	\$ 12,042	\$ 9,774

Appendix B – Demographic Information, By Diagnosis Group

		Asthma		Crohn's Disease		Chronic Pain		COPD	
		n	%/ SD	n	%/ SD	n	%/ SD	n	%/ SD
Total		83,161	100%	23,045	100%	82,183	100%	269,614	100%
Gender	Male	30,165	36.3%	10,056	43.6%	31,723	38.6%	106,815	39.6%
	Female	52,996	63.7%	12,989	56.4%	50,460	61.4%	162,799	60.4%
Average Age	Mean / Std	37.0	20.0	40.2	15.2	48.6	11.0	44.5	16.0
Age Group	Less than 18	21,702	26.1%	2,294	10.0%	998	1.2%	26,800	9.9%
	18 - 34	9,855	11.9%	5,660	24.6%	8,683	10.6%	33,525	12.4%
	35 - 44	12,051	14.5%	4,542	19.7%	14,659	17.8%	42,908	15.9%
	45 - 54	19,079	22.9%	5,678	24.6%	28,232	34.4%	74,062	27.5%
	56 - 64	20,474	24.6%	4,871	21.1%	29,611	36.0%	92,319	34.2%
Region	South	34,280	41.2%	9,064	39.3%	32,131	39.1%	119,815	44.4%
	Midwest	15,604	18.8%	5,200	22.6%	18,601	22.6%	65,054	24.1%
	Northeast	18,162	21.8%	5,010	21.7%	10,464	12.7%	43,585	16.2%
	West	13,697	16.5%	3,246	14.1%	19,740	24.0%	36,898	13.7%

		Cystic Fibrosis		Hepatitis C		Hypercholesterol		Immunodeficiency	
		n	%/ SD	n	%/ SD	n	%/ SD	n	%/ SD
Total		924	100%	2,097	100%	76,125	100%	611	100%
Gender	Male	552	59.7%	1,273	60.7%	38,087	50.0%	257	42.1%
	Female	372	40.3%	824	39.3%	38,038	50.0%	354	57.9%
Average Age	Mean / Std	35.3	18.5	53.3	8.6	54.2	19.2	46.4	19.2
Age Group	Less than 18	-	0.0%	-	0.0%	-	0.0%	-	0.0%
	18 - 34	181	19.6%	-	0.0%	1,080	1.4%	66	10.8%
	35 - 44	94	10.2%	145	6.9%	6,647	8.7%	81	13.3%
	45 - 54	162	17.5%	654	31.2%	24,902	32.7%	114	18.7%
	56 - 64	145	15.7%	1,197	57.1%	43,438	57.1%	147	24.1%
Region	South	276	29.9%	938	44.7%	31,257	41.1%	192	31.4%
	Midwest	155	16.8%	379	18.1%	18,036	23.7%	94	15.4%
	Northeast	154	16.7%	440	21.0%	14,516	19.1%	148	24.2%
	West	143	15.5%	324	15.5%	11,033	14.5%	107	17.5%

		Multiple Sclerosis		Osteoporosis		Psoriasis		Rheumatoid Arthritis	
		n	%/ SD	n	%/ SD	n	%/ SD	n	%/ SD
Total		15,031	100%	13,604	100%	31,214	100%	44,688	100%
Gender	Male	3,677	24.5%	194	1.4%	14,541	46.6%	14,193	31.8%
	Female	11,354	75.5%	13,410	98.6%	16,673	53.4%	30,495	68.2%
Average Age	Mean / Std	44.6	10.9	56.0	5.5	44.2	13.8	47.7	12.2
Age Group	Less than 18	-	0.0%	-	0.0%	1,716	5.5%	-	0.0%
	18 - 34	2,539	16.9%	71	0.5%	5,464	17.5%	4,430	9.9%
	35 - 44	4,192	27.9%	415	3.1%	6,268	20.1%	7,913	17.7%
	45 - 54	4,887	32.5%	3,780	27.8%	9,090	29.1%	14,399	32.2%
	56 - 64	3,077	20.5%	9,331	68.6%	8,676	27.8%	15,060	33.7%
Region	South	5,798	38.6%	6,191	45.5%	11,330	36.3%	18,618	41.7%
	Midwest	3,378	22.5%	2,369	17.4%	6,067	19.4%	8,845	19.8%
	Northeast	2,902	19.3%	2,435	17.9%	7,325	23.5%	7,154	16.0%
	West	2,431	16.2%	2,420	17.8%	5,953	19.1%	7,593	17.0%

Appendix C – Diagnoses Used to Identify Patients within Cohorts

Disease State	ICD-9 Diagnosis Code	ICD-10 Diagnosis Code
Rheumatoid Arthritis	714.0, 714.1, 714.2, 714.81, 720.0	M06.x, M05.x, L40.52, M45.x, M08.1, M48.8Xx, M45.9; M46.00;M46.1;M49.80;M46.90
Crohn's Disease	555.0	K50.x
Multiple Sclerosis	340.x	G35.x
Chronic Obstructive Pulmonary Disorder	490-492, 494, 496	J40.x, J41.0, J41.1, J41.8, J42.x, J43.9, J44.0, J44.1, J44.9
Cystic Fibrosis	277.0	E84.x
Immunodeficiency	279.x	D80.x - D84.x, D89.810, D89.811, D89.812, D89.813, D89.3, D89.4x, D89.89, D89.9, M35.9
Chronic Pain	338.2	G89.21, G89.22, G89.28, G89.29
Psoriasis	696	L30.5, L40.0, L40.1, L40.2, L40.3, L40.4, L40.5x, L40.8, L40.9, L41.8, L42.x, L44.0, L44.8, L45
Extrinsic Asthma (Allergic Asthma)	493.0	J45.20, J45.30, J45.40, J45.50, J45.909, J45.22, J45.32, J45.42, J45.52, J45.902, J45.21, J45.31, J45.41, J45.51, J45.901
Hepatitis C	070.51, 070.54	B18.2, B17.10
Hypercholesterolemia	272.0	E78.0x
Osteoporosis	733.0	M81.0, M81.6, M81.8

Appendix D – Medications Used in Switching Analysis

Table D1 – Chronic Medications for Treating Asthma

Generic Drug Name	Line Count	Mean Payment	St Dev Payment
Prednisone	76,797	\$ 5	\$ 71
Albuterol Sulfate	158,721	\$ 35	\$ 74
Montelukast Sodium	143,594	\$ 48	\$ 107
Fluticasone Propionate	78,684	\$ 52	\$ 200
Fluticasone Furoate	3,347	\$ 80	\$ 44
Ciclesonide	4,512	\$ 179	\$ 257
Budesonide / Formoterol Fumarate	31,036	\$ 200	\$ 124
Tiotropium Bromide	12,947	\$ 230	\$ 103
Fluticasone Propionate / Salmeterol Xinafoate	61,516	\$ 235	\$ 213

Table D2 – Chronic Medications for Treating Crohn's Disease

Generic Drug Name	Line Count	Mean Payment	St Dev Payment
Sulfasalazine	7,812	\$ 19	\$ 19
Azathioprine	20,533	\$ 27	\$ 49
Budesonide	19,230	\$ 995	\$ 643
Certolizumab Pegol	2,601	\$ 2,866	\$ 1,818
Adalimumab	23,068	\$ 3,369	\$ 3,043
Golimumab	373	\$ 4,028	\$ 2,851
Natalizumab	139	\$ 4,267	\$ 3,830
Infliximab	15,359	\$ 4,656	\$ 4,189
Ustekinumab	106	\$ 6,899	\$ 7,066
Vedolizumab	33	\$ 7,238	\$ 5,434
Rituximab	201	\$ 11,512	\$ 11,558

Table D3 – Chronic Medications for Treating Chronic Pain

Generic Drug Name	Line Count	Mean Payment	St Dev Payment
Oxymetazoline Hydrochloride	6	\$ 18	\$ 44
Guaifenesin	5	\$ 19	\$ 6
Gabapentin	214,861	\$ 60	\$ 282
Morphine Sulfate	86,376	\$ 103	\$ 504
Acetaminophen / Hydrocodone Bitartrate	9,779	\$ 153	\$ 102
Celecoxib	32,807	\$ 173	\$ 107
Fentanyl	65,234	\$ 202	\$ 393
Oxycodone Hydrochloride	228,885	\$ 215	\$ 411
Acetaminophen / Butalbital / Caffeine	1,074	\$ 235	\$ 173
Tramadol Hydrochloride	90	\$ 961	\$ 795

Table D4 – Chronic Medications for Treating COPD

Generic Drug Name	Line Count	Mean Payment	St Dev Payment
Prednisone	387,185	\$ 4	\$ 44
Ipratropium Bromide	22,786	\$ 74	\$ 240
Olodaterol	28	\$ 76	\$ 43
Albuterol Sulfate / Ipratropium Bromide	59,812	\$ 166	\$ 314
Umeclidinium	54	\$ 170	\$ 43
Formoterol Fumarate/Mometasone Furoate	27,761	\$ 213	\$ 269
Tiotropium Bromide	98,378	\$ 223	\$ 74
Umeclidinium Bromide / Vilanterol Trife	977	\$ 229	\$ 81
Aclidinium Bromide	5,630	\$ 270	\$ 713
Glycopyrrolate	27	\$ 314	\$ 383
Budesonide	42,997	\$ 376	\$ 333

Table D5 – Chronic Medications for Treating Cystic Fibrosis

Generic Drug Name	Line Count	Mean Payment	St Dev Payment
Azithromycin	62	\$ 129	\$ 121
Amylase / Lipase / Protease	2,445	\$ 1,137	\$ 1,255
Dornase Alfa	963	\$ 2,872	\$ 1,297
Tobramycin	388	\$ 5,080	\$ 2,567
Ivacaftor / Lumacaftor	8	\$ 21,386	\$ 943
Ivacaftor	87	\$ 26,446	\$ 3,810

Table D6 – Chronic Medications for Treating Hepatitis C

Generic Drug Name	Line Count	Mean Payment	St Dev Payment
Ritonavir	639	\$ 276	\$ 131
Ribavirin	6,305	\$ 473	\$ 427
Peginterferon Alfa-2B	744	\$ 2,736	\$ 749
Peginterferon Alfa-2A	5,508	\$ 2,799	\$ 1,657
Daclatasvir	8	\$ 22,454	\$ 993
Ledipasvir / Sofosbuvir	1,157	\$ 32,919	\$ 8,263

Table D7 – Chronic Medications for Treating Hypercholesterolemia

Generic Drug Name	Line Count	Mean Payment	St Dev Payment
Simvastatin	253,830	\$ 7	\$ 95
Lovastatin	31,007	\$ 7	\$ 28
Gemfibrozil	15,099	\$ 12	\$ 26
Fluvastatin Sodium	1,300	\$ 103	\$ 40
Fenofibric Acid	16,790	\$ 108	\$ 38
Ezetimibe / Simvastatin	18,832	\$ 118	\$ 39
Ezetimibe	33,538	\$ 123	\$ 42
Niacin	21,999	\$ 137	\$ 113
Amlodipine Besylate / Atorv	3,790	\$ 144	\$ 58
Alirocumab	5	\$ 488	\$ 668

Table D8 – Chronic Medications for Treating Immunodeficiency

Generic Drug Name	Line Count	Mean Payment	St Dev Payment
Hyqvia	74	\$ 44	\$ 57
Gamimune	2	\$ 80	\$ 70
Vivaglobin	5	\$ 142	\$ 260
Hizentra	5,307	\$ 2,988	\$ 6,300
Octagam	1,757	\$ 3,930	\$ 3,492
Sandoglobulin	1,029	\$ 3,661	\$ 4,220
Bivigam	53	\$ 3,843	\$ 2,605
Gammagard	6,350	\$ 4,061	\$ 4,478
Gammaplex	188	\$ 4,031	\$ 2,817
Flebogamma	762	\$ 4,270	\$ 4,135
Privigen	2,731	\$ 5,424	\$ 7,694
Gammaked	4,607	\$ 5,025	\$ 5,284
Gamunex-C	618	\$ 6,524	\$ 12,633

Table D9 – Chronic Medications for Treating Multiple Sclerosis

Generic Drug Name	Line Count	Mean Payment	St Dev Payment
Prednisone	10,674	\$ 5	\$ 34
Prednisolone	45	\$ 59	\$ 162
Methylprednisolone	4,238	\$ 76	\$ 168
Interferon Beta-1B	5,685	\$ 4,107	\$ 1,345
Interferon Beta-1A	24,425	\$ 4,182	\$ 3,326
Teriflunomide	1,284	\$ 4,684	\$ 1,241
Glatiramer Acetate	27,341	\$ 4,698	\$ 6,413
Natalizumab	4,511	\$ 4,729	\$ 3,900
Peginterferon Beta-1A	109	\$ 4,923	\$ 1,556
Dimethyl Fumarate	6,450	\$ 4,995	\$ 1,006

Table D10 – Chronic Medications for Treating Osteoporosis

Generic Drug Name	Line Count	Mean Payment	St Dev Payment
Estropipate	529	\$ 4	\$ 5
Estradiol	37,794	\$ 49	\$ 74
Bazedoxifene Acetate/ Conjugated Est	56	\$ 75	\$ 15
Conjugated Estrogens	12,145	\$ 76	\$ 66
Zoledronic Acid	9	\$ 709	\$ 302
Denosumab	1,318	\$ 1,303	\$ 4,375
Teriparatide	6,467	\$ 1,398	\$ 1,820

Table D11 – Chronic Medications for Treating Psoriasis

Generic Drug Name	Line Count	Mean Payment	St Dev Payment
Methoxsalen	17	\$ 49	\$ 50
Fluocinolone Acetonide	12	\$ 168	\$ 180
Calcitriol	10,189	\$ 448	\$ 381
Tazarotene	2,572	\$ 458	\$ 715
Calcipotriene	26,189	\$ 486	\$ 417
Betamethasone Dipropionate / Calc	31,414	\$ 797	\$ 741
Ustekinumab	3,809	\$ 9,079	\$ 19,833

Table D12 – Chronic Medications for Treating Rheumatoid Arthritis

Generic Drug Name	Line Count	Mean Payment	St Dev Payment
Alefacept	1	\$ -	-
Gold Sodium Thiomalate	6	\$ 6	\$ 9
Sulfasalazine	30,863	\$ 15	\$ 14
Azathioprine	12,977	\$ 23	\$ 42
Methotrexate Sodium	206,767	\$ 32	\$ 162
Leflunomide	28	\$ 66	\$ 67
Mycophenolic Acid	20,684	\$ 67	\$ 138
Cyclosporine	351	\$ 320	\$ 267
Tacrolimus	3,856	\$ 326	\$ 353
Tofacitinib Citrate	1,269	\$ 2,001	\$ 3,752
Anakinra	1,056	\$ 2,095	\$ 2,217
Tocilizumab	1,767	\$ 2,355	\$ 2,219
Etanercept	46,440	\$ 2,431	\$ 2,222
Abatacept	4,040	\$ 2,533	\$ 2,005
Adalimumab	44,710	\$ 2,846	\$ 4,319
Golimumab	4,206	\$ 2,908	\$ 4,112
Certolizumab Pegol	3,101	\$ 2,971	\$ 1,959
Infliximab	15,489	\$ 4,425	\$ 5,081
Vedolizumab	21	\$ 8,170	\$ 6,294
Rituximab	1,687	\$ 10,486	\$ 10,578