Formulary Exclusion: Assessment of Medical Costs, Pharmacy Costs, and Resource Utilization Compared to a Concurrent Control Group

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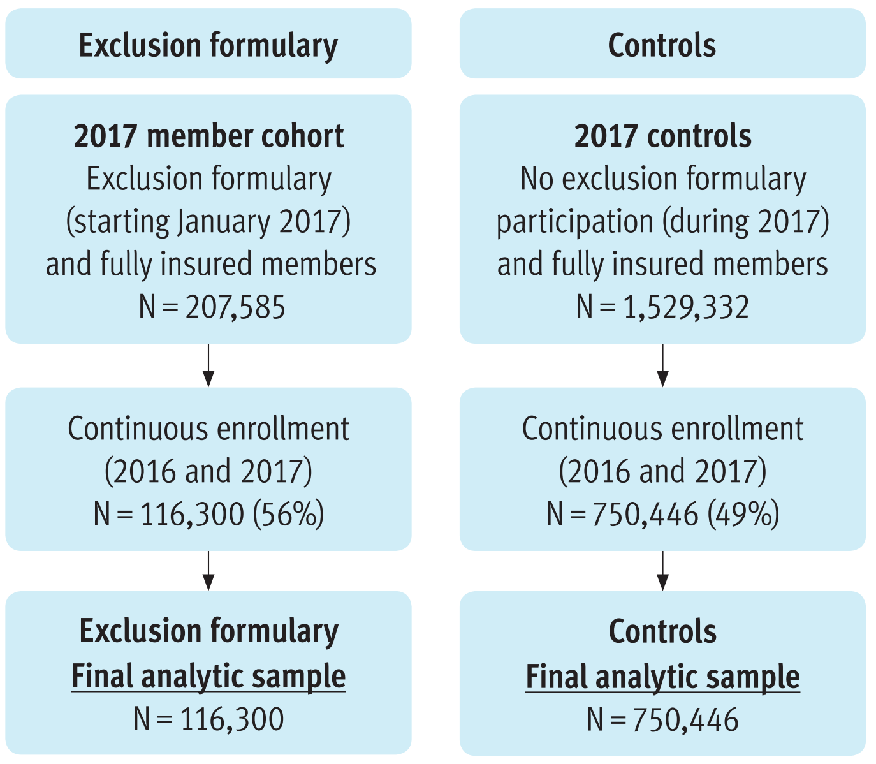
Background

- Formulary exclusions have emerged to address escalating drug expenditures.
- The goal of an exclusion formulary (EF) is to place select high-cost medications within a drug class that have clinically supported lower cost alternatives into a non-coverage status. Individuals and/or their provider may appeal non-coverage.
- On Jan. 1, 2017, four Blue Cross Blue Shield plans implemented an EF consisting of over 300 excluded drugs.
- Concern exists for increased medical resource utilization and cost impact associated with formulary restrictions.
- A 2016 meta-analysis examined 18 studies assessing 19 drug exclusion policies' impact on overall health care costs.[1]
  - Fourteen policies had reduced costs.
  - One policy had a neutral impact on costs.
  - Four policies had increased costs.
- Prime Therapeutics' (Prime) EF encourages cost-effective generic and preferred brand use. It is Prime's most comprehensive formulary management strategy to achieve the lowest pharmacy cost of care.[2]

Objectives

- Describe the impact of an EF on:
  - Medical resource utilization and total cost of care, defined comprehensively as all medical and pharmacy costs
  - Adherence to diabetes mellitus (DM) medications and beta-blocker medication for heart failure
  - Chronic condition (i.e., asthma, heart failure, and diabetes) medical resource utilization and total cost of care

Figure 1. Member Attrition Flow



Exclusion formulary	Controls
2017 member cohort Exclusion formulary (starting January 2017) and fully insured members N = 207,585	**2017 controls** No exclusion formulary participation (during 2017) and fully insured members N = 1,529,332
Continuous enrollment (2016 and 2017) N = 116,300 (56%)	Continuous enrollment (2016 and 2017) N = 750,446 (49%)
Exclusion formulary **Final analytic sample** N = 116,300	**Controls** **Final analytic sample** N = 750,446

Table 1. Baseline Characteristics

Characteristic	Exclusion formulary (N = 116,300)	Control (N = 750,446)	p – value
Age, years as of 1/1/2017 (mean)	36.8	38.2	‹0.01
Female	50.5%	48.1%	‹0.01
MSA Rural	8.2%	16.1%	‹0.01
Median household income* (mean)	$68,000	$69,678	‹0.01
Education, high school degree*	87.6%	88.7%	‹0.01
Race, white*	72.8%	78.6%	‹0.01
Charlson Score† in 2016 (mean)	0.139	0.142	0.04
Charlson Score 1 to 3	8.1%	7.7%	
Charlson Score 4+	0.5%	0.6%	

MSA, Metropolitan Statistical Area.

*ZIP code derived.

†Charlson Score is a 10-year mortality risk metric.

Table 3. Medical and Pharmacy Cost of Care Change from 2016 to 2017, Per Member Per Month (PMPM)

Total cost of care	Exclusion formulary (N = 116,300)	Control (N = 750,446)	Adjusted difference p – value
Overall*	2016 to 2017 Change	2016 to 2017 Change	
Overall pharmacy cost	0.2%	5.4%	p ‹ 0.01*
Overall medical cost	11.9%	12.7%	p = 0.69
Diabetes mellitus	**N = 5,923**	**N = 30,441**	
Overall pharmacy cost	−1.7%	5.3%	p ‹ 0.01*
Overall medical cost	7.1%	16.6%	p = 0.03
Asthma	**N = 6,512**	**N = 36,962**	
Overall pharmacy cost	−6.1%	1.4%	p = 0.31
Overall medical cost	−13.8%	−6.8%	p = 0.35
Heart failure	**N = 340**	**N = 4,164**	
Overall pharmacy cost	−4.1%	−2.8%	p = 0.91
Overall medical cost	−2.6%	−12.9%	p = 0.60

*Gamma distribution analysis cost comparisons.

All costs are insurer allowed amounts paid to provider after network discounts including member and plan paid.

Table 4. Medical Resource Utilization: Adjusted Outcomes, Incidence Rate Ratio

Utilization	Exclusion formulary (N = 116,300)	Control (N = 750,446)	Adjusted difference p – value
Overall*	Incidence rate ratio 2016 to 2017 change	Incidence rate ratio 2016 to 2017 change	Incidence rate ratio difference†
Emergency room visits	1.03	1.02	p = 0.52
Inpatient visits	1.10	1.07	p = 0.32
Outpatient/office visits	0.97	1.02	p ‹ 0.01*
Diabetes mellitus	**N = 5,923**	**N = 30,441**	
Emergency room visits	1.05	1.04	p = 0.88
Inpatient visits	1.05	1.07	p = 0.79
Outpatient/office visits	0.91	1.00	p ‹ 0.01*
Asthma	**N = 6,512**	**N = 36,962**	
Emergency room visits	0.84	0.85	p = 0.76
Inpatient visits	0.75	0.80	p = 0.53
Outpatient/office visits	0.84	0.90	p ‹ 0.01*
Heart failure	**N = 340**	**N = 4,164**	
Emergency room visits	0.84	0.85	p = 0.89
Inpatient visits	0.66	0.73	p = 0.48
Outpatient/office visits	0.78	0.88	p = 0.01*

*Negative binomial distribution analysis (count data). †Statistical adjustment for member characteristic differences between the two groups using generalized estimating equations.

Table 5. Members with Excluded Medications Drug Therapy Discontinuation in 2017

Drug category	Members with supply on Dec. 31, 2016	Members discontinuing (%)	p – value
Insulins excluded			
Controls†	482	37 (7.7%)	p = 0.49
Exclusion formulary	24	1 (4.2%)	
Diabetes mellitus drugs, all excluded products*			
Controls†	1,217	76 (6.2%)	p = 0.50
Exclusion formulary	171	13 (7.6%)	
Metformin containing excluded products			
Controls†	373	40 (10.7%)	p = 0.41
Exclusion formulary	79	11 (13.9%)	
Heart failure members with an excluded beta-blocker‡			
Controls†	42	8 (19.1%)	p = 0.58
Exclusion formulary	5	0 (0.0%)	

Discontinuation was defined as not having any drug supply in the category 270 days or later into the year.

†Control group drug utilizers with supply on Dec. 31, 2016, however in the Control group the drug was not excluded.

*Any excluded diabetes mellitus including expensive generics, insulins, amylin analogs, thiazolinodines (TZDs), branded metformin containing products, DDP4i (see below), and GLP-1 agonist (see below).

‡Excluded heart failure indicated beta-blockers: Coreg CR, carvedilol (ER), and Bystolic.

Methods

- The study design was a retrospective cohort with concurrent control using integrated medical and pharmacy administrative claims data.
- The EF was implemented on Jan. 1, 2017, for a subset of the four Blue plans' fully insured membership. The subset of fully insured membership that continued to use the standard formulary offering from Prime Therapeutics was identified as the control group.
- The statistical comparison method was a pre-post difference-in-difference to examine the EF group change in study outcomes from the pre-period (baseline) to the post-period and compare them to the changes in the control group (non-EF) using the same time periods.[3]
- The pre-period was defined as calendar year 2016, and the post-period was defined as calendar year 2017.

Study Population

- The analysis inclusion criteria were members from:
  - Four Blue Cross Blue Shield plans
  - Fully insured members continuously enrolled in 2016 and 2017:
    - EF members were identified as those who began the formulary on Jan. 1, 2017. Note: All members with formulary excluded drug supply were identified in the three months prior (October 2016) to the EF implementation on Jan. 1, 2017, and sent notification letters. A second notification letter was sent to members with formulary excluded drug supply in early December 2016.
    - Controls were members who did not implement the EF during calendar year 2017.
- Members with the following conditions were also evaluated separately: heart failure, DM, and asthma.
  - Members were identified as having heart failure or asthma if they had at least one claim with an International Classification of Diseases – Version 10 (ICD-10) from January 2016 through June 2016.
  - Specific to DM, we incorporated Healthcare Effectiveness Data and Information Set (HEDIS) criteria to identify members with any of the following from January 2016 through June 2016: 1) at least two DM outpatient visits, observation visits, emergency department (ED) visits or nonacute inpatient encounters on different dates of service; or 2) at least one acute inpatient encounter with a DM diagnosis.

Outcomes Measurement

- Total cost of care (medical and pharmacy allowed cost including provider and pharmacy network discounts) was examined for members by calculating the 2016 and 2017 average per member per month (PMPM) cost for members in the EF group compared to the control group.
- Utilization was examined by the number of outpatient/office visits, ER visits, and inpatient hospitalization stays in 2016 and 2017.
- Medication adherence was assessed by a 12-month proportion of days covered (PDC) calendar year difference-in-difference analysis. End of year PDC from 2016 and 2017 (separately) for members who met CMS Star Rating adherence measurement criteria were calculated. The changes in PDC were examined for the oral DM drugs.
- Drug discontinuation was defined as having no drug supply on and after Oct. 1, 2017, among members identified with formulary exclusion product supply on Dec. 31, 2016.
  - Excluded medications were identified by both National Drug Code (NDC) and Generic Product Identifier (GPI, from Medi-Span®).
  - Discontinuation within drug class and within the entire disease category was examined. The indicated heart failure beta blocker drug class utilizing members were also required to have a heart failure diagnosis in the first half of 2016.
  - DM drug classes were analyzed separately as well as pooled to create an all DM medications category.

Statistical Analysis

- SAS 9.4 (SAS Institute Inc., Cary, NC) was used for all analyses.
- For total cost of care, a general estimating equation (GEE) was fit with a gamma distribution adjusting for Blue plan, Charlson Index Score (severity of illness proxy), rural-urban, age, gender, and zip code derived sociodemographic variables.[4]
- For utilization, a GEE was fit with negative binomial distribution generating incidence rate ratios (IRRs).[5]
- Statistical significance for all analysis was set at p ‹ 0.01, due to large sample size and multiple comparisons.

Results

- On Jan. 1, 2017, members with comprehensive medical and pharmacy benefits were identified **(Figure 1).**
  - 207,585 fully insured EF members:
    - 116,300 (56 percent) meeting analytic criteria and continuously enrolled in 2016 and 2017
  - 1,529,332 fully insured non-EF members:
    - 750,446 (49 percent) meeting analytic criteria and continuously enrolled in 2016 and 2017
- 5,872 (5.0 percent) of 116,300 members had a formulary excluded product drug supply on Dec. 31, 2017, after two notifications. Of 5,872 members with any formulary-excluded drug:
  - 180 (3.1 percent) **asthma inhaler** excluded drug members
  - 171 (2.9 percent) **DM** excluded drug members
  - 5 (0.0 percent) **heart failure and beta-blocker** excluded drug members
- 4,119 (70.1 percent) of 5,872 members with an excluded drug were in six drug categories:
  - 1,218 (20.7 percent) of 5,872 members utilized antihypertensive and lipid lowering (e.g., 3-omega fatty acid)
  - 887 (15.1 percent) gastrointestinal (e.g, acid reducers)
  - 706 (12.0 percent) stimulants (e.g., amphetamine products)
  - 454 (7.7 percent) ophthalmic (e.g, dry eye products)
  - 438 (7.5 percent) allergic rhinitis
  - 416 (7.1 percent) dermatologic
- Baseline characteristics were statistically different between the groups, primarily as a result of the large analytic populations. Of note, the EF group was on average 1.5 years younger, had a higher percentage of females, lived in more rural ZIP codes, and had a higher percentage of whites compared to the control group **(Table 1).** All characteristics were adjusted for in the statistical multivariate models.
- With total cost of care, we found a statistically significant, 2016 to 2017, 5 percentage point decrease in all pharmacy cost PMPM for the EF group compared to the control group **(Table 3).**
- EF all medical cost PMPM was 1 percentage point lower, not statistically significant, 2016 to 2017, compared to the control group **(Table 3).**
- Assessing medical utilization, we did not find a statistically significant difference from pre- to post-period between the two groups for ER and inpatient visits **(Table 4).**
- The EF group showed a statistically significant 5 percent lower incidence in outpatient and office visits compared to the control group **(Table 4).**
- Members with heart failure and asthma had results consistent with overall medical utilization and medical costs, i.e., no difference in medical costs, ER or inpatients visits **(Tables 3 and 4).**
- For DM members, the EF group showed a statistically significant decrease in pharmacy PMPM compared to controls **(Table 5).** A decrease was also seen for medical PMPM **(Table 5).** Medical utilization analyses found the change pre- to post-period showed no statistically significant difference between the two groups for ER and inpatient visits.
- No difference in adherence or discontinuation with excluded medications analyzed was seen **(Table 5).**

Table 2. Excluded Drugs and Members Counts with Supply on Dec. 31, 2016

Excluded drug supply on Dec. 31, 2016	Exclusion formulary (N = 116,300)	Control (N = 750,446)‡
Diabetes mellitus medications*	171	1,217
Heart failure diagnosis and Beta-blocker†	5	42
Insulin by drug (specific products listed below by brand name)		
Apdira	4	54
Afrezza	0	5
Basaglar	0	1
Humalog	17	376
Humalog mix	2	19
Humulin 70/30	0	17
Humulin N	2	7
Humulin R	0	9
Insulin total	**24**	**482**
metformin expensive generics and metformin branded products, including combinations	79	373
DPP-4i	9	37
GLP-1 agonist	9	43

*Any excluded diabetes mellitus including expensive generics, insulins, amylin analogs, thiazolinodines (TZDs), branded metformin containing products, DDP4i (see below), and GLP-1 agonist (see below).

†Excluded heart failure indicated beta-blockers: Coreg CR, carvedilol (ER), and Bystolic.

‡Control group drug utilizers with supply on Dec. 31, 2016, however in the Control group the drug was not excluded.

DPP4i = dipeptidyl peptidase 4 inhibitor excluded products: alogliptin containing products (e.g.,Nesina, Oseni) .

GLP-1 agonist = glucagon-like peptide-1 excluded product: exenatide containing products (e,g, Byetta).

Limitations

- Administrative pharmacy and medical claims have the potential for miscoding and include assumptions of members' actual diagnoses and utilization.
- The asthma, DM, and heart failure medical resource utilization and total cost of care analysis included all members with a diagnosis and was not limited to those impacted by a formulary-excluded drug. The inclusion of all members with a chronic condition instead of only those affected by a formulary exclusion may have impacted the finding.
- It is unknown what other cost savings or utilization programs were occurring among the four Blue Cross Blue Shield fully insured populations. If other programs were put in place, they would have applied to both the EF and control groups, as all members analyzed in both groups were fully insured, not self-insured.
- Medication adherence and discontinuation assessments have the potential for misclassification bias due to an inability to assess whether members are paying cash for their medication or receiving medication from pharmaceutical manufacturer patient assistance programs, thus erroneously declaring a member as discontinuing their medication due to an incomplete record via administrative claims.
- The DM medication adherence comparison used the CMS Star adherence measure method and included all members in the analysis group using an oral diabetes medication, including members that did not have a formulary-excluded product supply in the pre-period, which may have impacted the findings.
- Many of the discontinuation and adherence assessments' comparisons had a small number of members, usually less than 100, and in some instances, less than 20 members. These small numbers, coupled with the multiple comparisons limited statistical power to determine if a difference existed.
- Only members continuously enrolled for two years were assessed, introducing potential bias as members may have disenrolled secondary to being notified their medication was no longer being covered by their insurance.

Conclusions

- To our knowledge, this is the first large comprehensive assessment of an exclusion formulary (EF) on medical resource utilization, total cost of care and medication adherence.
- Although 1 in 20 members had a supply of an excluded formulary (EF) product after two notifications, at the date of EF implementation, only 0.3 percent of members had an asthma, DM or heart failure beta-blocker excluded product.
- 70 percent of all impacted members were utilizers of expensive generic or brand antihypertensive, lipid lowering, gastrointestinal (e.g., acid reducers), stimulants, ophthalmic, allergic rhinitis or dermatologic products.
- The analysis of a large commercial fully insured population newly implemented on an EF of over 300 drugs found no associated medical resource utilization or medical benefit cost increase with an associated statistically significant pharmacy benefit cost savings compared to a large concurrent commercial fully-insured control group within the same Blue plans.
- In the first year that the exclusion formulary was implemented (2017), members who were continuously enrolled for two years (2016 to 2017) were found to have:
  - A 5 percentage point decrease in pharmacy costs from 2016 to 2017, compared to a control group and no difference in medical costs.
  - No difference in overall inpatient stays or ER visits with a slightly lower statistically significant outpatient/office visits incidence rate compared to a control group.
- Chronic conditions: asthma, DM and heart failure analyses found:
  - No statistically significant differences in medical care resource utilization or costs, and lower pharmacy costs compared to controls.
  - Medication adherence and discontinuation were not statistically different between the two groups for DM and heart failure. Asthma was not evaluated due to known difficulty in assessing inhaler adherence and discontinuation.
- Commercial insurers should consider implementation of an EF to control pharmacy costs and conduct further impact analyses. This study found no associated increase in medical resource or cost with the Prime EF.

Strengths

- The fully insured members used in both the EF and control group were from the same four Blue Cross Blue Shield plans.
- We examined a two-year period with integration of medical and pharmacy claims and repeated outcome assessment of the same member, difference-in-differences assessments with concurrent control group.

References

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