

Pharmacoeconomic Impact of Inhaled Corticosteroids

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Abstract

Inhaled corticosteroids (ICSs) are recommended by the National Heart, Lung, and Blood Institute as first-line treatment for persistent asthma, whether mild, moderate, or severe. Available data consistently show that ICSs offer the best outcomes for management of asthma. Economic analyses comparing fluticasone with triamcinolone and zafirlukast are presented in this study. These data show that treatment with fluticasone results in decreased hospitalizations and emergency department visits and better cost savings, as measured by asthma care costs and total healthcare costs, despite being more expensive than triamcinolone, and that zafirlukast is more expensive than fluticasone and is a less effective in lowering medical costs.

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because the studies were not powered to measure them; emergency department (ED) visits and hospitalizations do not commonly occur in that time frame. Economic analyses are also limited in that only drug costs or cost modeling from the clinical trials were reviewed.⁸ While every clinical study has certain limitations, the consistency of the data from studies of different asthma medications is striking. The consistency is observed in both subjective and objective measurements and translates into the economic analyses presented in this paper.

The focus of the managed care industry is to improve quality and decrease variation in healthcare delivery while realizing cost savings. The analyses presented here use data from a managed care organization, United Healthcare, to look at the healthcare use associated with asthma therapies in a realistic population and the costs associated with each.

Study Design

The study objective was to demonstrate that the findings of clinical efficacy correlate with what is observed in real-world practice. Using United Healthcare data from administrative claims, the study used a decision tree of selecting one therapy versus another. Data from patients identified as having asthma by the *International Classification of Diseases*, 9th Revision (ICD-9) code (493.XX) were used. The analyses examined the effect of each of the 3 therapies on rates of ED visits, hospitalizations, costs of asthma care, and

Numerous clinical studies have demonstrated the benefits of inhaled corticosteroids (ICSs) for the treatment of persistent asthma, but the studies have limitations.¹⁻⁷ Most were short-term studies (4 to 12 weeks) using carefully selected patients. Overall, exacerbation data from these studies are inconclusive

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total costs of care (Table 1). All patients were enrolled for at least 21 months: 9 months pre-index and 12 months post-index. The index event was the first prescription for an ICS, either fluticasone or triamcinolone, or a leukotriene modifier, zafirlukast, during an 18-month observation period. Patients could not have a claim for an ICS or leukotriene modifier in the 9-month, pre-index period. During the post-index period, they could not use the alternative medication (ie, any other ICS or leukotriene modifier). All healthcare claims, including those that were asthma related, were captured during the pre- and post-index periods. They included hospitalizations and charges, ED visits and charges, physician office visits and charges, outpatient visits and charges, and all asthma related and total pharmacy claims (using National Drug Codes). Analysis of covariance and multiple linear regression were performed to control for the covariates. The mean monthly costs and rates were adjusted for age and sex, the pre-index healthcare costs, asthma costs, comorbid respiratory conditions, β_2 -agonist use, and all corticosteroid use as well as pre-index hospitalizations, ED visits, physician visits, and outpatient rates.

This study had several limitations. Only patients with an ICD-9 code for asthma were included. Patient selection bias was associated with the method of patient selection (ie, only those taking fluticasone, zafirlukast, or triamcinolone). Disease severity was controlled for in the multiple covariate analysis.

Comparing Fluticasone and Zafirlukast

Studies have shown that zafirlukast, a leukotriene modifier, is effective in improving pulmonary function and decreasing asthma symptom scores, nighttime awakenings, and supplemental albuterol use.⁹⁻¹¹ Leukotriene modifiers are considered an

alternative therapy to low-dose ICS for mild persistent asthma, as described in the 1997 guidelines from the National Heart, Lung, and Blood Institute (NHLBI) on diagnosis and management of asthma, but its more specific role has not been fully established. Clinical experience and evaluation will help to determine which patients will benefit most from this type of therapy.¹²

The first analysis compared 3 doses of fluticasone with zafirlukast. The distribution of dosage strength in the fluticasone groups was: 28% used the 44- μg dose, 49.3% used the 100- μg dose, and 22.2% used the 220- μg dose. Analyses using only the 2 lower doses revealed similar results to those using the full patient population.

After adjusting for age and gender, the patient demographics between the 2 treatment groups were quite

Table 1. Study Design

<ul style="list-style-type: none"> ■ Administrative claims cohort database ■ 13 geographically diverse, United Healthcare-affiliated plans, insuring 1.4 million lives ■ Study period: October 1, 1995, through December 31, 1998 ■ Pre-index period of 9 months and post-index period of 12 months. Patients were continuously enrolled for at least 21 months ■ Costs were calculated on a per-treated-patient per-month basis

The index event was the first prescription for an inhaled corticosteroid or leukotriene modifier.

Table 2. Patient Demographics: Fluticasone Versus Zafirlukast

	Fluticasone Propionate	Zafirlukast
Number	1101	392
Age (\pm SD)	34.2 (\pm 17.1)	39.0 (\pm 15.9)
Gender (M/F)	41/59	45/65

similar (Table 2). Zafirlukast patients tended to be older, which was corrected for by subanalyses.

Pre-index asthma drug costs were slightly lower for patients treated with fluticasone, but this was adjusted for in the analysis. Zafirlukast is more expensive than fluticasone, therefore asthma drug costs were higher with zafirlukast overall by \$9.45 per member per month (PMPM).

Emergency department visit rates revealed a statistically significant difference between the 2 treatment groups. Patients treated with fluticasone had a 62% reduction in ED visits versus a 32% reduction in those taking zafirlukast. Similarly, hospitalization rates showed a 70% versus 26%

decrease in patients treated with fluticasone and zafirlukast, respectively. Interestingly, the pre-index hospitalization rates for both treatment groups were very similar. These results are consistent with another study using health maintenance organization (HMO) data comparing all ICS and cromolyn sodium.¹³

Total asthma care costs, including costs of hospitalizations, ED visits for asthma, drugs, and office visits, showed similar marked differences. While costs for asthma care decreased by \$13 PMPM with fluticasone, they increased by \$13 PMPM with zafirlukast (Table 3). The difference in total asthma costs is approximately \$320 per year less for fluticasone versus zafirlukast.

Zafirlukast is more expensive than fluticasone, and this data suggests that it is less effective in reducing medical costs.

The total healthcare costs show a similar but more striking trend. Total healthcare costs decreased by 6% for patients treated with fluticasone but increased by 24% for those treated with zafirlukast. The difference in total costs is significantly higher than what could be accounted for by the asthma care costs alone (Table 3).

Other studies of children enrolled in HMOs indicate that the total nonasthma healthcare costs are higher in children with asthma than in children who do not have asthma.¹⁴ Some of these costs could be attributed to illnesses such as bronchitis or pneumonia, which are not coded as asthma but may be related to the underlying disease. All of the outcomes measurements clearly indicate that fluticasone offers better asthma control at a lower cost than zafirlukast (Table 4).

Table 3. Asthma Care Costs and Total Healthcare Costs: Fluticasone Versus Zafirlukast

	Asthma Care Costs (\$)			Total Healthcare Costs (\$)		
	Pre-index	Post-index	Difference	Pre-index	Post-index	Difference
FP	59.53	46.33	-13.20*	334.40	312.93	-21.47†
ZA	63.43	76.82	13.39	306.07	380.18	74.11

FP = fluticasone propionate; ZA = zafirlukast.

Asthma care costs declined 22% for patients treated with FP while rising 21% for ZA. Total healthcare costs declined by 6% for patients treated with FP while rising 24% for ZA.

**P* < 0.001.

†*P* < 0.02.

Table 4. Fluticasone Versus Zafirlukast—A Summary

Fluticasone	Zafirlukast
70% decrease in hospitalizations	26% decrease in hospitalizations
62% decrease in ED visits	32% decrease in ED visits
Asthma costs decreased: \$158/y	Asthma costs increased: \$161/y
Total healthcare costs decreased: \$258/y	Total healthcare costs increased: \$889/y

ED = emergency department

Fluticasone Versus Triamcinolone

Fluticasone has demonstrated superior efficacy over triamcinolone in clinical trials regarding peak expiratory flow rate (PEFR), rescue albuterol use, and withdrawals because of lack of efficacy.¹⁵ In this study, these 2 drugs were compared in a study designed similarly to the previous one except that only the 2 lower doses of fluticasone (44 and 110 µg) were used, allowing for similar baseline demographics (Table 5). The results were maintained if all fluticasone patients were studied

The acquisition costs of fluticasone are greater than triamcinolone (a difference of \$9.02 vs \$6.46 PMPM, fluticasone versus triamcinolone, between post- and pre-index asthma drug costs, *P* < 0.001). However, asthma care costs declined significantly more for fluticasone than triamcinolone treatment (\$126 per year with fluticasone versus \$47 per year with triamcinolone, *P* < 0.02).

Pre-index ED use rates were essentially the same between the 2 treatment groups, but fluticasone patients had a 59% decrease versus a 38% decrease for triamcinolone patients. Asthma-related hospitalization rates declined 64% for fluticasone and only 29% for triamcinolone. The overall difference was significant (*P* < 0.01).

Asthma care costs decreased 21% for patients treated with fluticasone versus 10% for those treated with triamcinolone. For total healthcare costs, a 9% decrease was seen with fluticasone, even though it is a more expensive drug, versus a 13% increase for triamcinolone. Fluticasone was associated with better outcomes, fewer ED visits and hospitalizations, and showed the greatest reduction in both total asthma and total healthcare costs. Clinical studies show that fluticasone offers greater improvement in lung function and symptom control compared with triamcinolone.¹⁵ This study validates the superiority of fluti-

casone with lower hospitalization rates, ED rates, and decreased costs when patients were followed for 12 months (Table 6).

The Reality of Patients' Drug Use for Asthma

A closer look at the dosing of ICSs in this population provides an example of the difference between real-world drug use and clinical trial dosing. For those receiving zafirlukast, the average number of monthly refills was approximately 5.3 per year, for fluticasone it was 4.3 per year, and for triamcinolone, it was 3.6 per year; this shows that refill rates were not at the levels expected or desired by the prescribing physicians.

Compliance is also an issue that affects outcomes and costs. Patients take their medications when they perceive they need to. Previously published data indicate that fluticasone has a rapid onset of action; change in baseline PEFR occurs within the first

Table 5. Patient Demographics: Fluticasone Versus Triamcinolone

	Fluticasone Propionate (44/110 µg)	Triamcinolone
No. patients	857	4142
Age (±SD)	32.9 (±17.6)	34.6 (±17.0)
Gender (M/F)	42/58	39/61

Fluticasone	Triamcinolone
64% decrease in hospitalizations	29% decrease in hospitalizations
59% decrease in ED visits	38% decrease in ED visits
Asthma costs decreased: \$126/y	Asthma costs decreased: \$47/y
Total healthcare costs decreased: \$324/y	Total healthcare costs increased: \$375/y

ED = emergency department

week and lung function improves by 50% within 2 weeks and by 90% within 3 weeks.¹⁶ While patients are attentive enough to take the drug when they perceive the disease flaring up, acknowledging that this is not the ideal way of taking medicine, this method seems to work. In comparing fluticasone with zafirlukast, despite somewhat lower compliance with fluticasone use, the outcomes are better. Compliance with a drug that is not as effective adds cost but may not improve outcomes.

... CONCLUSION ...

Clinical studies have clearly shown the therapeutic benefits of ICSs in treating persistent asthma. Hence, ICSs are recommended as first-line treatment for persistent asthma at all levels of severity. Because clinical studies are, by definition, controlled environments, they only offer insight into the short-term efficacy; for asthma therapy, that is 4 to 12 weeks. The final question, after efficacy is established, is whether a drug is effective in the real world. Typical asthma patients are not as well monitored as those in clinical trials, they have comorbid conditions, and their compliance is not likely to be as high. The data presented here reflect a real-world study of what transpires in a clinical setting, and patients are followed over a 12-month period, allowing better realization of drug efficacy.

The relative clinical data on asthma therapies has been consistent. The economic analyses presented here confirm the advantage of ICSs, and in particular, fluticasone, in terms of outcomes that can be measured economically: drug costs, asthma care costs, ED use, and hospitalization rates. Again, these data are consistent with clinical trial data. Fluticasone achieves better outcomes and is less expensive overall, in terms of asthma

care costs and total healthcare costs, than zafirlukast. In addition, fluticasone appears to be superior to triamcinolone when assessing these same outcome parameters.

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