

Treating allergic rhinitis in patients with comorbid asthma: The risk of asthma-related hospitalizations and emergency department visits

Jodi Crystal-Peters, BA, Cheryl Neslusan, PhD, William H. Crown, PhD, and
Amelito Torres, MA *Washington, DC*

Background: Although asthma and allergic rhinitis commonly occur together, the nature of the association has yet to be determined. Treatments for one condition could potentially alleviate the coexisting condition.

Objective: Patients with both allergic rhinitis and asthma were studied to test the hypothesis that treating allergic rhinitis reduces health care utilization for co-morbid asthma.

Methods: A retrospective cohort study was carried out with 1994-1995 MarketScan claims data. The cohort was limited to patients with both allergic rhinitis and asthma, aged 12 to 60 years, who were continuously enrolled and had no evidence of chronic obstructive pulmonary disease. Allergic rhinitis treatment and asthma-related events (hospitalizations and emergency department visits) were identified. An incidence density ratio (IDR) associated with exposure to allergic rhinitis treatment was calculated. A multivariate Poisson regression was estimated, and the parameter estimates were transformed into IDRs for each explanatory variable. An allergic rhinitis treatment indicator was included in all regressions.

Results: The study sample population consisted of 4944 patients with allergic asthma, approximately 73% of whom were treated for their allergic rhinitis. Asthma-related events occurred more often for the untreated group compared with the treated group, 6.6% compared with 1.3%. An IDR of 0.49 for the treatment group ($P = .001$) indicates that the risk of an asthma-related event for the treated group was about half that for the untreated group.

Conclusion: In summary, those who were treated for allergic rhinitis have a significantly lower risk of subsequent asthma-related events (emergency department visits or hospitalizations) than those who were not treated. (*J Allergy Clin Immunol* 2002;109:57-62.)

Key words: Allergic rhinitis, asthma, administrative claims analysis

Evidence supporting a relationship between asthma and allergic rhinitis has been broadly discussed in the clinical literature. Epidemiologic data show that allergic rhinitis (AR) and asthma frequently co-exist. AR is high-

Abbreviations used

AR: Allergic rhinitis
ED: Emergency department
IDR: Incidence density ratio

ly comorbid with asthma.¹ Asthma has been found in 19% to 38% of persons with a history of AR but only 3% to 5% of the general population. As many as 78% of patients with asthma report nasal allergy symptoms, well above the 20% rate in the general population.² Moreover, treatments that relieve nasal symptoms of AR and asthma also reduce the pulmonary symptoms of allergic asthma.³

Symptoms of rhinitis can include nasal discharge, nasal blockage, sneezing, and itching. Asthma symptoms include episodic breathlessness, wheezing, chest tightness, and a cough that may worsen at night. Although the main treatment for AR is allergen avoidance aimed at reducing exposure, pharmacotherapy is often used to terminate the inflammatory process.⁴ Pharmacotherapies for AR include decongestants, antihistamines, intranasal cromolyn, and topical nasal corticosteroids. Topically sprayed (intranasal) corticosteroids and nasal cromolyn are examples of drugs used to suppress the inflammatory process. Antihistamines and decongestants are examples of agents used to relieve symptoms of AR.

Recent studies suggest that appropriate treatment of AR reduces asthma symptoms. Pharmacotherapy for AR may result in diminishing asthma symptoms, increasing airway caliber, and decreasing bronchial hyperresponsiveness. It has been suggested that using an antihistamine alone or using an antihistamine with a decongestant results in the reduction of asthma symptoms.^{3,5} A study conducted by Grant et al⁶ showed that asthma symptoms were reduced in patients with AR treated with an antihistamine as compared with patients who did not receive treatment. Treatment of rhinitis has the potential to reduce asthma symptoms to such an extent that treatment with prophylactic anti-asthma drugs may be unnecessary in some patients with a diagnosis of mild asthma.

Although AR and asthma commonly occur together, clinicians have yet to determine the exact nature of the association between these two chronic conditions. Exposure to allergens seems to be a critical factor in the development of AR and asthma. Because incidence and prevalence rates for both diseases have been increasing,^{7,8}

From The MEDSTAT Group, Washington, DC.

Supported by Integrated Therapeutics Group, Inc., a subsidiary of Schering Plough.

Received for publication April 5, 2000; revised September 24, 2001; accepted for publication September 24, 2001.

Reprint requests: Jodi Crystal-Peters, The MEDSTAT Group, 4401 Connecticut Ave, NW, Suite 400, Washington, DC 20008.

Copyright © 2002 by Mosby, Inc.

0091-6749/2002/\$35.00 + 0 1/81/120554

doi:10.1067/mai.2002.120554

effective treatment for both diseases would benefit a large segment of the population. Once the link between AR and asthma is established, treatments for one condition could potentially alleviate the coexisting condition.

Halpern et al⁹ observed that patients with symptomatic rhinitis were receiving more asthma medications, especially more inhaled and supplemental corticosteroids, as compared with the general population. In their examination of the effects of intranasal corticosteroids in patients with chronic perennial AR and mild asthma, Henriksen and Wenzel¹⁰ found that 4 weeks of therapy significantly reduced both rhinitis and asthma symptoms.⁹ Welsh et al¹¹ found that patients with AR receiving intranasal corticosteroids also experience a reduction in lower airway symptoms attributed to asthma. Watson et al¹² found that intranasal corticosteroid therapy reduced both rhinitis and asthma symptoms yet showed that less than 2% of the drug was deposited in the lower airways.

Because topically applied nasal steroids have not been shown to result in significant deposition to the lungs, the reduction in asthma symptoms may be related to improvements in nasal function as opposed to the direct effects of the medication on the lower airway.⁵ This implies that reflex interactions between the upper and lower airways, which have been demonstrated in animal models, may be relevant in human airway disease.¹³ Also, the tools of molecular biology have provided us an insight into the cellular basis of the allergic inflammatory reaction. The initial allergic insult to the nose results in cell mediator and cytokine release. The subsequent recruitment of secondary cells involved in the persistent allergic inflammatory cascade may result in recruitment of eosinophils, basophils, and lymphocytes to the entire respiratory tract and not just to the nasal mucosa.¹¹

Because AR is implicated in the pathogenesis of asthma, it has been hypothesized that the management of AR would be likely to result in the alleviation of asthmatic symptoms.³ Reducing asthma symptoms with therapy for rhinitis can potentially decrease asthma-related health care resource utilization and the associated costs. In this article we focus on two particular resource utilization measures, emergency department (ED) visits and hospitalizations for treatment of asthma. The purpose of this study was to assess the relationship between prescription medication use for the treatment of AR and subsequent asthma-related ED visits and hospitalizations for patients with AR and comorbid asthma. We test the hypothesis that the treatment of AR among patients diagnosed with AR and asthma results in significantly fewer asthma-related ED visits and inpatient admissions.

METHODS

Data

The analytical file used in this study was constructed from the 1994-1995 MarketScan databases (The MEDSTAT Group, Inc, Ann Arbor, Mich). MarketScan contains data on more than 4 million covered lives annually, representing the health-care experiences of privately insured persons employed in large companies or organizations and the covered dependents of those employees. Contributors

to MarketScan come from all areas of the country but are concentrated in the north central and southern areas of the United States. In general, the plans are operated as indemnity-type or preferred provider organization network health insurance programs.

The database links paid claims and prescription drug data to detailed patient, provider health plan, and enrollee information. Historically, more than 500 million claims records have been available in the MarketScan databases, and the databases are available as far back as 1988. The databases include diagnosis, procedure, provider, site of care, benefit plan, and payment information for each medical claim submitted by participating self-insured employers. Outpatient prescription drug data—National Drug Code, therapeutic class, ingredient cost, dispensing fee, co-payment, deductible, total gross payment, and other data elements—are available for a subset of the total MarketScan population.

Study population

We identified patients from the subset of the 1994 MarketScan database with prescription drug data available who had both AR and asthma. Individuals were classified as having both asthma and AR if they had at least one diagnosis for each condition and at least one prescription for a β -agonist during 1994. Those patients without an asthma diagnosis on their medical claims but at least two prescription claims for β -agonists were also "flagged" as asthmatic. Patients without an AR diagnosis were classified as having AR if they had at least two pharmacy claims for non-sedating antihistamines, nasal inhaled steroids, or both during 1994. It should be noted that although patients with an AR diagnosis and no prescriptions for AR medications were flagged as AR cases, asthma cases were required to have at least one asthma medication. An asthma medication was required because of the uncertainty associated with the coding of an asthma diagnosis.

Patients who were continuously enrolled in their health plan for the study period were identified by using enrollment data and a claims-based proxy for enrollment. Using the enrollment data available for a subset of the population, we identified those patients who had a positive enrollment flag during 1994 and 1995. For the rest of the sample, we flagged patients as continuously enrolled if they incurred any service claims during the first and last quarters of the study period. Patients who were not continuously enrolled were excluded from the analytical sample. Patients younger than 12 years or older than 60 years, those with chronic obstructive pulmonary disease, and those with missing analytic variables were also excluded from the sample. Younger patients (<12 years) were excluded because other variables could confound the diagnosis of asthma in this population.

The 1994 database include information on 31,728 patients with asthma, 73,411 with AR, and 12,208 with both conditions. After all data exclusions were applied, there were 4944 patients in the final study population.

Analysis variables

The analysis variables were constructed by using the 1995 claims experience of the patients included in the analytical sample. Study periods were constructed based on the first asthma-related ED visit or hospital admission observed during 1995. The study period was defined as either the time between January 1, 1995, and December 31, 1995, or the time between January 1, 1995, and the date of the first asthma-related ED visit or hospitalization.

We created a variable that indicated whether an individual was treated for AR during the study period. An individual was considered treated if he or she had a prescription for a nasal inhaled steroid, a sedating antihistamine, or a non-sedating antihistamine. The total exposure time was calculated for each patient to control for the varying length of time that an individual was at risk for an

event. For the treated cohort, exposure time was calculated by counting the actual number of months in which an AR prescription was filled in the study period, and for the untreated cohort, the exposure time was the total number of months in the study period.

The dependent variable in the analysis was an asthma-related event. We defined asthma-related events for the treated cohort as hospitalizations or ED visits occurring during the study period but within 31 days after a prescription for AR medication to strengthen the association between AR treatment and asthma-related events. For the untreated cohort, an event was defined as any hospitalization or ED visit for treatment of asthma that occurred any time during the study period.

Statistical methods

We computed descriptive statistics and associated χ^2 tests of significance to determine whether differences exist between the treated and untreated cohorts in terms of demographics and prior utilization of health care services. Next, to estimate the magnitudes of the associations between exposure to risk factors and the number of asthma-related events in the population, we calculated incidence density ratios (IDRs). This measure of relative risk indicates the likelihood of an event in the exposed group relative to the unexposed group, adjusted for the time that each individual was at risk for an event. The IDR is a ratio of two incidence rates: $(a/N1)/(b/N2)$, where a and b represent the number of cases and $N1$ and $N2$ represent the cumulative exposure time in the exposed and unexposed groups, respectively.¹⁴

We first calculated an IDR associated with exposure to AR treatment. IDRs were also calculated for asthma-related events for exposure to each potential confounder. These included demographics (age and sex), the number of comorbid conditions (major diagnostic categories), and proxies for asthma severity. These proxies included the following resource utilization measures in 1994:

- Prior asthma-related ED visit
- Prior asthma-related inpatient admission
- Number of β -agonist prescriptions in 1994
- Number of orally inhaled steroid prescriptions in 1994
- Oral steroid use in 1994
- Theophylline use in 1994
- Cromolyn use in 1994

Next, we estimated a multivariate Poisson regression model to simultaneously control for effects of these potential confounding factors on the number of events in the population. Poisson regression was used to estimate a model that examined the counts of asthma-related events in the study population. The parameter estimates from the Poisson regression were transformed into IDRs by exponentiating each coefficient.^{15,16} The main variable of interest was an indicator for AR treatment. Chi-square statistics were used to test for significant relationships between the independent factors and asthma-related events.

RESULTS

The prevalence of asthma in the 1994 MedRx MarketScan database is approximately 6% and the prevalence of AR is 13%. Approximately 2% of the MarketScan population had both asthma and AR. In our final study population of 4944 patients with both conditions, approximately 73% of the patients were treated for AR. Of those who were treated, 86% ($n = 3083$) received at least one antihistamine and 76% ($n = 2718$) received at least one nasal inhaled steroid.

TABLE I. Comparison of population treated for allergic rhinitis with population not treated for allergic rhinitis: Demographics, asthma medication patterns, and asthma-related resource utilization

	Treated (n = 3587)		Untreated (n = 1357)	
	No.	% of total	No.	% of total
Demographics				
Age (y)				
12-20	666	18.6	430	31.7
21-30	292	8.1	124	9.1
31-40	707	19.7	246	18.1
41-60	1922	53.6	557	41.0
Sex				
Male	1250	34.8	537	39.6
Female	2337	65.2	820	60.4
1994 Asthma medication patterns				
β -Agonist				
1-6	2632	73.4	1022	75.3
7+	955	26.6	335	24.7
Inhaled steroids				
0	1858	51.8*	784	57.8
1-6	1358	37.9	496	36.6
7+	371	10.3	77	5.7
Oral steroids				
No	2319	64.7	925	68.2
Yes	1268	35.3*	432	31.8
Theophylline				
No	2769	77.2	1052	77.5
Yes	818	22.8	305	22.5
Cromolyn				
No	2868	80.0	1114	82.1
Yes	719	20.0	18	17.9
1994 Asthma-related resource utilization				
ED				
0	3476	96.9	1279	94.3
1	91	2.5*	60	4.4
2+	20	0.6*	18	1.3
Hospitalization				
No	3556	99.1	1326	97.7
Yes	31	0.9*	31	2.3

ED, Emergency department.

*Significant differences between treated and untreated cohort where $P < .01$.

Table I compares the subjects who were treated for AR with those who were not treated. Members of the treated group were significantly more likely to be female ($P = .002$) and older than those of the untreated group ($P = .001$). The drug utilization patterns in 1994 are compared. Patients who were treated for AR had significantly higher numbers of prescriptions for orally inhaled steroids than those who were not treated. Nearly 52% of the treated group had no prescription for orally inhaled steroids as compared with 57.8% of the untreated group ($P = .001$). A similar prescription pattern was found for use of other oral steroids. Approximately 35% of the treated group had any prescription for an oral steroid in 1994 compared with nearly 32% of the untreated group ($P = .02$). However, no statistically significant differences were found in the use of β -agonists, theophylline, and cromolyn between the treated and untreated groups.

TABLE II. Association between demographics, confounders/severity variables, and events-bivariate analysis

	IDR	95% CI	P value
Allergy treatment			
Untreated population	—	—	—
Treated population	0.49	.34-.69	.0001
Age (y)			
12-20			
21-30	1.18	.67-2.03	.54
31-40	0.78	.48-1.25	.32
41-60	0.52	.35-.80	.002
Sex			
Male			
Female	1.3	.91-1.88	.1504
β-Agonist			
1-6			
7+	3.15	2.26-4.40	.0001
Inhaled steroids			
0			
1-6	1.6	.63-2.10	.008
7+	1.19	1.13-2.27	.56
Oral steroids			
0			
1+	2.58	1.85-3.62	.0001
Theophylline			
0			
1+	2.8	2.00-3.90	.0001
Cromolyn			
0			
1+	2.25	1.58-3.17	.0001
ED			
0			
1	10.01	6.50-14.93	.0001
2+	17.4	9.07-30.37	.0001
Inpatient			
0			
1+	8.94	4.92-14.97	.0001
MDC count			
1-3	0.58	.32-1.14	.09
4-9	0.67	.39-1.27	.185
10+			
Sinusitis			
No			
Yes	1.23	.87-1.74	.24
Otitis media			
No			
Yes	0.87	.27-2.07	.79

Source: Tabulation of 1994-95 MarketScan data.

IDR, Incidence density ratio; ED, emergency department; MDC, major diagnostic category.

The baseline ED and hospitalization rates for the treated and untreated groups were very similar. The likelihood of an ED visit or hospitalization in 1994 was significantly lower among those who were treated for their AR in 1995 relative to the untreated group. Prior ED utilization was 3.1% among the treated group versus 5.7% in the untreated group ($P = .001$). Similarly, less than 1% of the treated group had a prior hospitalization compared with 2.3% of the untreated group ($P = .001$).

In the bivariate analyses presented in Table II, the relationship between each of the covariates and asthma-related events was estimated by using IDRs. The magnitude and statistical significance of the estimated IDRs are useful for identifying factors associated with elevated risk of ED and hospitalization events. In particular, statistically significant IDRs with a value greater than 1 imply that members of groups with that characteristic have a higher risk of ED visits or hospitalizations than those who do not have that characteristic. Conversely, statistically significant IDRs less than 1 imply that members of groups with that characteristic have a lower risk of ED visits or hospitalizations.

The IDR for the treatment group was 0.49 ($P = .001$). This point estimate indicates that the risk of an asthma-related event for the treated group was about half that of the untreated group. Many of the other variables representing potential confounding factors were also statistically significant. Subjects in the following groups were at a significantly higher risk of having had an asthma hospitalization or ED visit in 1995:

- Those with more than 7 β-agonist prescriptions in 1994
- Those with 1 to 6 orally inhaled steroid prescriptions in 1994
- Those who had any prescriptions for oral steroids in 1994
- Those who had any prescriptions for theophylline in 1994
- Those who had any prescriptions for cromolyn in 1994
- Those who had an asthma-related ED visit in 1994
- Those with an asthma-related inpatient stay in 1994

These results indicate that as the severity of asthma increases, the risk of asthma-related events increases as well. The bivariate analysis examines the independent relationship of each of these factors to the asthma events. However, because many of the potential confounders were found to be significant, it was important to estimate the treatment effect in a multivariate context. The variables to be included in the model were determined a priori, and insignificant variables were not excluded from the final model specification. Table III presents the pooled multivariate regression models comparing the number of asthma-related events (ED visits or hospitalizations) in the study sample by selected characteristics. Most of the factors that were considered related to an increase in asthma-related events in the bivariate analysis were also found to be significant in the multivariate analysis. The relationship between oral inhaled steroid use and asthma-related events is not consistent across the two analyses. Although not significant in the multivariate analysis, the adjusted IDR for having prescriptions for 1 to 6 orally inhaled steroids indicates that there may be a slight increase in the risk of asthma-related events. However, as shown in Table III, when controlling for covariates, having more than 7 prescriptions for inhaled steroids decreases the risk of asthma-related events significantly.

In general, the findings are consistent in terms of sign and significance with the descriptive findings. In fact, in models that examined ED and hospitalization variables

separately (not shown), there were no substantive differences in the magnitude of the IDRs. Most importantly, in all 3 analyses, treatment for AR was significantly associated with a lower risk of asthma-related events even when the effect of the other confounders was considered.

DISCUSSION

The main result of this study is that those who were treated for AR have a significantly lower risk of subsequent asthma-related events (ED visits or hospitalizations) than those who were not treated. Qualitatively similar results were found for the risk of hospitalizations for treatment of asthma. The magnitude of the effect of treatment on both events is quite large. The prevented fraction among those exposed to treatment was 47% (1-IDR). These results imply that 47% of subjects who were treated for their AR did not have an asthma-related event when we control for other observable characteristics.

The relationship between sinusitis and asthma is well documented in the literature.¹⁷⁻¹⁹ Therefore, it was expected that having a diagnosis of sinusitis would affect the likelihood of having an asthma-related event. However, the presence of sinusitis was not significant in the bivariate analysis and barely approached significance in the multivariate analysis ($P = .06$). It may be that although sinusitis and asthma commonly occur together, the presence of sinusitis does not significantly exacerbate the symptoms of asthma.

Of course, these results should be interpreted in context and are subject to the usual limitations faced by any retrospective analysis based on claims data. In this study we identified patients with AR and asthma with algorithms that utilized *International Classification of Diseases 9th Revision, Clinical Modification* (ICD-9-CM) codes and prescription claims data. It is important to acknowledge that diagnostic information provided by ICD-9-CM codes may not be consistently reliable or valid because of inaccurate coding of diagnoses. Errors may occur in the transcription of medical records to discharge forms and claims records. Further, coding may be influenced by reimbursement incentives, or the diagnoses themselves may be incorrect. These limitations require the development of an algorithm that draws on information from procedure codes, drug codes, or both to identify cases for analysis of treatment patterns and expenditures. Additional evidence, beyond diagnostic codes, associated with treatment for a particular medical condition reduces the probability that cases are incorrectly included or excluded from retrospective analyses that use administrative claims data.

In addition to diagnoses for asthma and AR, this study incorporated prescription medication use into the patient identification algorithm. It is still possible that this study sample includes individuals who have been misdiagnosed or who are taking the identified medications for a reason other than the treatment of AR or asthma. Medications that can be purchased without a prescription are often used in the treatment of AR. Individuals with AR

TABLE III. Multivariate results comparing the number of asthma events in the study sample by selected characteristics

	Adjusted IDR	95% CI	P value
Untreated population	—	—	—
Treated population	0.53	.36-.76	.0001
Age (y)			
12-20			
21-30	0.98	.54-1.71	.03
31-40	0.93	.56-1.53	.79
41-60	0.61	.40-.96	.95
Sex			
Male			
Female	1.19	.82-1.76	.37
β-Agonist			
1-6			
7+	2.2	1.50-3.23	.0001
Oral inhaled steroids			
0			
1-6	1.06	.73-1.54	.74
7+	0.52	.26-.98	.05
Oral steroids			
0			
1+	1.3	.89-1.91	.17
Theophylline			
0			
1+	1.88	1.10-2.14	.0007
Cromolyn			
0			
1+	1.48	1.30-2.70	.043
ED			
0			
1	5.82	3.65-9.04	.0001
2+	7.76	3.91-14.00	.0001
Inpatient			
0			
1+	4.14	2.22-7.18	.0001
MDC count			
1-3	0.73	.47-1.60	.36
4-9	0.84	.38-1.48	.57
10+			
Sinusitis			
No			
Yes	1.41	.98-2.00	.06

Source: Tabulation of 1994-95 MarketScan data.

IDR, Incidence density ratio; ED, emergency department; MDC, major diagnostic category.

who use only these over-the-counter medications in the treatment of their AR could not be identified in the MarketScan database if they did not have a doctor's visit for AR. Therefore, the sample in this study may be an underrepresentation of the true study population.

It is also important to note that the treated population in this study consists of individuals who received antihistamines and nasally administered corticosteroids. Given that these treatments differ in mechanism of action, it is possible that they would have different effects on asthma outcomes. Given that approximately 61% of the patients in this study received both types of treatments, the potential differences would not affect these results significant-

ly. However, future studies exploring the effects of alternative treatment modalities may provide additional insight into the relationship between AR and asthma.

Another limitation that should be considered is the possibility that those who were prescribed medication for AR were different from those who were not in ways that could not be observed in claims data. These unobserved differences (eg, unobservable asthma disease severity) may be explanatory factors associated with differences in the risk of asthma-related events.

A variety of methods can be used to reduce the bias introduced by confounding variables (both observed and unobserved).²⁰ The most effective method is a randomized clinical trial. The present study used Poisson regression to control for the effects of observed variables that might confound inferences about the effects of AR treatment on the risk of asthma-related events. Future work could control for the effects of unobserved variables as well, through either a randomized clinical trial or use of established statistical methodologies.

REFERENCES

1. American Academy of Allergy, Asthma and Immunology. Fast facts: statistics on asthma and allergic diseases. Available from: URL: <http://www.aaaai.org/public/fastfacts/statistics.stm>
2. Pedersen PA, Weeke ER. Asthma and allergic rhinitis in the same patients. *Allergy* 1983;38:25-9.
3. Fireman P. Rhinitis and asthma connection: management of coexisting upper airway allergic diseases and asthma. *Allergy Asthma Proc* 2000;21:45-54.
4. Lemaske RF. A review of the current guidelines for allergic rhinitis and asthma. *J Allergy Clin Immunol* 1998;101:S392-S396.
5. Corren J. The impact of allergic rhinitis on bronchial asthma. *J Allergy Clin Immunol* 1998;101:S352-S356.
6. Grant JA, Nicodemus CF, Findlay SR, Glovsky MM, Grossman J, Kaiser H, et al. Cetirizine in patients with seasonal rhinitis and concomitant asthma: prospective, randomized, placebo-controlled trial. *J Allergy Clin Immunol* 1995;95:923-32.
7. Rowe-Jones JM. The link between the nose and lung, perennial rhinitis and asthma—is it the same disease? *Allergy* 1997;52(suppl 367):20-8.
8. Sly RM. Changing prevalence of allergic rhinitis and asthma. *Ann Allergy Asthma Immunol* 1999;82:233-52.
9. Halpern M, Richner R, Togias A, et al. Allergic rhinitis may increase asthma costs [abstract]. *Am J Respir Crit Care Med* 1996;153:A860.
10. Henriksen JM, Wenzel A. Effect of an intranasally administered corticosteroid (budesonide) on nasal obstruction, mouth breathing, and asthma. *Am Rev Respir Dis* 1984;130:1014-8.
11. Welsh PW, Stricker WE, Chu CP, Naessens JM, Reese ME, Reed CE, et al. Efficacy of beclomethasone nasal solution, flunisolide, and cromolyn in relieving symptoms of ragweed allergy. *Mayo Clin Proc* 1987;62:125-34.
12. Watson WT, Becker AB, Simons FE. Treatment of allergic rhinitis with intranasal corticosteroids in patients with mild asthma: effect on lower airway responsiveness. *J Allergy Clin Immunol* 1993;91(1 Pt 1):97-101.
13. Busse WW. Current research and future needs in allergic rhinitis and asthma. *J Allergy Clin Immunol* 1998;101:S424-426.
14. Hennekens CH, Buring JE. *Epidemiology in Medicine*. Boston Little, Brown and Company; 1987.
15. StataCorp. *Stata Statistical Software: release 5.0 reference Manual*. Stata Press, College Station (TX): Stata Corporation; 1997.
16. Selvin S. *Statistical analysis of epidemiologic data*. 2nd ed. New York: Oxford University Press; 1996.
17. Altemeier WA III, Graff GR. How are allergic rhinitis and sinusitis connected with asthma? *Pediatr Ann* 2001;29:391-2, 398.
18. Skoner DP. Complications of allergic rhinitis. *J Allergy Clin Immunol* 2000;105:S605-S609.
19. Bykowski M. The role of allergy in the development of otitis media and sinusitis. *J S C Med Assoc* 2000;96:229-31.
20. Heckman J. The common structure of statistical models of truncation, sample selection, and limited dependent variables and a simple estimator for such models. *Ann Economic Social Measurement* 1976;5:475-92.