Impact of Inhaled Corticosteroid–Induced Oropharyngeal Adverse Effects on Treatment Patterns and Costs in Asthmatic Patients: Results from a Delphi Panel

Michael Kaliner, MD, Alpesh Amin, MD, MBA, Ronald Gehling, MD, PharmD, Concetta Crivera, PharmD, Evelyn Chiao, PharmD, Tejal Vishalpura, PharmD, and Thomas Bramley, PhD

ABSTRACT

Inhaled corticosteroids (ICSs) are associated with rare systemic adverse drug effects (ADEs) but, more commonly, are associated with oropharyngeal ADEs. The objective of this study was to determine the treatment patterns employed by physicians for ICS-induced oropharyngeal ADEs in order to ultimately determine their economic burden.

A panel of 15 physicians completed three rounds of a Delphi process to validate the “seeding” algorithm, to assess initial probabilities of the algorithm, and to facilitate consensus on those probabilities. After consensus was achieved, costs were assigned to office visits.

The most commonly reported ADE was oral candidiasis (5.6%), followed by cough (5.3%), sore throat (4.8%), and dysphonia (4.1%). The mean number of office visits needed to diagnose and treat cough was 3.4; dysphonia, 3.3 visits; sore throat, 2.5 visits; and oral candidiasis, 1.9 visits. The panel estimated that 26% to 30% of patients required a dose reduction and that 14% to 29% needed to be switched to another ICS. Cough was the most costly ICS-induced ADE ($154 million); oral candidiasis was the least costly ($91 million).

The total economic burden for office visits associated with ICS-induced ADEs was approximately $464 million. ICS-induced oropharyngeal ADEs can be associated with a significant economic burden as a result of increased physician time.

INTRODUCTION

Asthma is a common respiratory disease that affects approximately 20 million adults and children in the U.S. The economic burden of asthma in the U.S. is between $6 billion and $10 billion annually, primarily as a result of direct medical costs. Asthma has a significant impact on health care costs and physician time in the U.S.; in 2001, patients made more than 11 million physician office visits, and in 2002, there were almost 2 million emergency room visits and 465,000 hospitalization days for asthma management.

Drug therapy to control asthma symptoms includes inhaled corticosteroid (ICS) agents, short-acting and long-acting beta-agonists, leukotriene modifiers, cromoglicate, theophylline, anti–immunoglobulin G (IgE) antibodies, and oral corticosteroids. Treatment guidelines have been developed to facilitate decisions regarding drug therapy according to asthma severity.

ICSs are the cornerstone of asthma therapy; between 37% and 83% of patients with persistent asthma reportedly use an ICS agent. The National Asthma Education and Prevention Program (NAEPP) has established ICSs as the preferred treatment for all patients with persistent asthma; low-dose ICSs for mild, persistent asthma; low-to-medium dose ICSs for moderate, persistent asthma; and high-dose ICSs for severe, persistent asthma. ICSs, however, can be associated with local and systemic adverse drug effects (ADEs). Systemic ADEs, such as hypothalamic–pituitary–adrenal suppression, bone loss, cataracts, and growth retardation in children, can be prevented by titrating to the lowest effective dose or by switching to a less potent ICS.

Local ADEs occur mainly in the oropharynx and include oropharyngeal dysphonia, sore throat, oral candidiasis, and cough. ADEs are often viewed clinically as a class effect of all ICS agents and are often considered minor in comparison to systemic ADEs. However, local ADEs can be associated with patient discomfort and potential noncompliance with the prescribed ICS therapy.

The incidence of ICS-related oropharyngeal ADEs is at least 3% in clinical trials of current single-entity ICS products.

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approved for use in the U.S., namely triamcinolone (Azmacort®, Kos), budesonide (Pulmicort®, AstraZeneca), beclomethasone (Qvar® 3M), fluticasone (Flovent® Rotadisk®, GlaxoSmithKline), and flunisolide (Aerobid®, Forest).15–19 The incidence of these ADEs is greater for combination products, such as fluticasone/salmeterol (Advair®, GlaxoSmithKline).20

A review of the literature shows that the incidence of ICS-related oropharyngeal ADEs varies from 1% to 17%, depending on the ADE and the ICS dose. Clinical trials in adolescents and adults with asthma have revealed an incidence of oral candidiasis from 2% to 17% (with high-dose, dry-powder, inhalation ICS agents), dysphonia from 1% to 11%, and pharyngitis from 1% to 4%.21–24

Observational studies, however, report relatively higher rates. A survey of 213 pulmonologists and allergists reported that the frequency of oropharyngeal symptoms (hoarseness, sore throat, and oral candidiasis) was “occasional” in 48% of patients and “frequent” in 3% of patients, although the range of incidence was not defined.25 In adults, more than 50% of patients using an ICS reported dysphonia, and more than 30% of patients reported cough.26

A survey in 639 children conducted by Dubus and colleagues reported cough in 39.7% of those using an ICS, hoarseness in 14.1%, and oral candidiasis in 10.7%.14 In a different study, Dubus et al., specifically investigating cough in children, found that more than 50% of these patients had an ICS-induced cough regardless of the agent, dose, or inhalation device.13 Approximately 20% of these children had a reduced rate of compliance because of the cough, and they often required a return visit to the physician’s office for further evaluation or a change in therapy.13

These observational studies suggest that ICS-related oropharyngeal ADEs occur more frequently than reported in product package inserts; they may prompt physician office visits, and they have the potential to reduce patient compliance. However, the prevalence of localized ADEs reported in the current literature does not reflect the actual number of patients actively seeking medical care; consequently, the actual number of care-seeking patients is not known, and the impact of ICS-induced oropharyngeal ADEs on subsequent health care utilization has not yet been quantified.

The purpose of this study was to assess treatment patterns and probabilities of ICS-induced oropharyngeal ADEs to estimate the economic burden associated with consequent physician office visits.

METHODS

Delphi Panel Process

The Delphi process is used to identify evidence that is best determined from group involvement or an expert panel. Types of research for which the Delphi process is appropriate include:27

- exploring underlying perceptions that lead to treatment differences.
- assembling information on diverse aspects of

a topic (e.g., topics spanning many different disciplines).
- seeking to form consensus from opinion.

The Delphi process may be used to develop consensus guidelines for complex therapeutic problems. We used a Delphi process for this study because this type of data was lacking in claims databases. Although International Classification of Diseases (ICD-9) codes do exist for conditions such as cough, oral candidiasis, throat pain, and dysphonia, they are generic in etiology. We could have used a claims database to determine the attributable risk of ADEs by selecting a control group for comparison with patients treated with ICS, but we thought that such analysis would be confounded by both the disease state (asthma) and by the severity of the disease state. For example, cough is a symptom of asthma, and cough is also related to the severity of asthma; this makes it difficult to select an appropriate control group without biasing results. The Delphi process is an effective broad-based method of gathering information that is not readily available in claims databases.

For this study, we used a modified Delphi process in which the anonymity of panel members was maintained; however, the questions in the first round were structured rather than open-ended. The purpose of the Delphi process was to bring about consensus on the diagnostic and treatment patterns and likelihood of oropharyngeal ADEs occurring in patients treated with an ICS.

Panel members were required to see at least 10 patients who used an ICS each month and to have at least one year of prac-

A Non-consensus

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B Consensus

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<td>40%</td>
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<td>17%</td>
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Figure 1 Consensus of probabilistic assessment. This figure shows how the use of the interquartile range (IQR) of 20% or below determines consensus. For each item on the survey requesting probabilities, the range of responses varied from 0% to 100%. A, When the IQR (the difference between the 25th and 75th percentile) was greater than 20%, consensus was not achieved. B, When the IQR was 20% or less, consensus was achieved.
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We assessed the number of office visits needed to diagnose ADEs in two ways, in an attempt to further isolate only those ADEs induced by the ICS agent. Panel members were directly asked (1) to report the number of visits to determine whether an ADE was ICS-induced in a traditional survey format and (2) to apply percentages to the branches of an algorithm evaluating the number of visits to diagnose the ADE in an open-ended survey format.

We also asked the panel members to apply percentages to the branches of algorithms in Figures 3 and 5 to diagnose ICS-induced ADEs and to treat or follow up ICS-induced ADEs until resolution of symptoms or referral of the patient to another specialist. These percentages were then used to determine the total number of office visits (“four” or more was considered to be four office visits). We summed the greater number of office visits needed to diagnose the ADEs based on the algorithm or the open-ended survey and the number of office visits needed to treat until symptom resolution or referral to another specialist, whichever was greater, to obtain an upper limit around each ADE. We used a similar method to obtain a lower limit for each ADE. The midpoint of the upper limit and the lower limit was used as the mean number of office visits.

### Table 1 Characteristics of Delphi Panel Members

<table>
<thead>
<tr>
<th>Description</th>
<th>No. of Physicians</th>
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<tr>
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</tr>
<tr>
<td>Academic institution</td>
<td>3</td>
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<tr>
<td>Allergist</td>
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<tr>
<td>Pulmonologist</td>
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<td><strong>Geographical region</strong></td>
<td></td>
</tr>
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<td>Northeast</td>
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</tr>
<tr>
<td>South</td>
<td>3</td>
</tr>
<tr>
<td>West</td>
<td>6</td>
</tr>
</tbody>
</table>
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Economic Burden

Figure 2 illustrates how the economic burden was determined for the ICS-induced ADEs. We used epidemiological data, such as the prevalence data from the Centers for Disease Control and Prevention (CDC) and the Verispan Physician Drug and Diagnosis Audit, to determine the population using ICS agents. We determined the frequency of ADEs and the utilization of resources from the results of the Delphi process.

We computed the cost of the office visits using the 2004 Physicians’ Fee and Coding Guide. The total economic burden was calculated as the sum of the economic burden of each oropharyngeal ADE. Monte Carlo simulations were used to perform sensitivity analyses on our results.

RESULTS

Sixteen physicians participated in round one of the Delphi Panel process. One physician declined further participation after the first round, and the remaining 15 physicians returned all questionnaires. The distribution of panel members is shown in Table 1.

After the first round, nasal congestion and sinusitis were dropped as ADEs because the panel did not consider them to be representative of oropharyngeal events. Sore throat ultimately replaced pharyngitis because of the similarities in patient presentation and management. The final oropharyngeal ADEs of interest were cough, oral candidiasis, dysphonia, and sore throat.

Panelists reported that ICS-induced ADEs resulted in care-seeking in 3% to 6% of their asthma patients for whom an ICS had been prescribed. The most commonly reported ADE was oral candidiasis (5.6%), followed by cough (5.3%), sore throat (4.8%), and dysphonia (4.1%).

Results from the treatment algorithms show that diagnosis of an ICS-induced ADE was often determined within two office visits or by a phone call from the physician for most patients (Table 2). The panel reported that three or more visits were required to determine the cause of cough in almost 20% of patients and to determine the cause of dysphonia in almost 9% of patients.

The mean number of office visits needed to diagnose an ICS-induced ADE based on the treatment algorithms was as follows: 1.5 visits for cough, one visit for oral candidiasis, 1.2 visits for dysphonia, and one visit for sore throat (Table 3). The validated seeding algorithms for diagnosis, treatment, and follow-up for ICS-induced ADEs are provided in Figures 3 to 5 (see pages 580 to 582).

When results from the treatment algorithm and the open-ended survey were compared, the results were similar for the number of office visits needed to diagnose ICS-induced ADEs. The survey revealed 2.1 visits for cough, one visit for oral candidiasis, 1.5 visits for dysphonia, and 1.6 visits for sore throat (see Table 3). We summed these results with the mean number of office visits reported to treat the ADEs until symptoms were resolved or until referral to another specialist, determined from the treatment algorithms, as described in the methods and from Tables 3 and 4.

For instance, to determine the upper limit of physician office visits needed to diagnose and manage cough, the mean of 2.1 visits to diagnose cough (from the survey) was summed with the mean of 1.6 visits to treat to referral, or a total of 3.7 visits. The mean of 1.5 visits to diagnose cough (from the algorithm) was summed with the mean of 1.5 visits to treat to symptom resolution, for a lower limit of three visits. We calculated the midpoint value (3.4 visits) from these. Sensitivity analyses (see next page) account for the uncertainty of the estimated number of office visits for each of the ADEs, and they address the robustness of the estimates.

As illustrated in Table 4, cough was perceived as requiring the most office visits to diagnose and treat (3.4 visits) compared with oral candidiasis (1.9 visits), dysphonia (3.3 visits),
Inhaled Corticosteroid–Induced Adverse Effects

Table 5 Reported Cost of Physician Office Visits for Inhaled Corticosteroid–Induced Adverse Drug Effects in the U.S.

<table>
<thead>
<tr>
<th></th>
<th>Cough</th>
<th>Oral Candidiasis</th>
<th>Dysphonia</th>
<th>Sore Throat</th>
<th>Total</th>
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<tr>
<td>Total No. of office visits</td>
<td>2,998,168</td>
<td>1,770,283</td>
<td>2,251,121</td>
<td>1,996,560</td>
<td>9,016,132</td>
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<tr>
<td>Cost of office visit</td>
<td>$51.50</td>
<td>$51.50</td>
<td>$51.50</td>
<td>$51.50</td>
<td>$51.50</td>
</tr>
<tr>
<td>Total cost</td>
<td>$154,405,652</td>
<td>$91,169,575</td>
<td>$115,932,732</td>
<td>$102,822,840</td>
<td>$464,303,798</td>
</tr>
</tbody>
</table>

and sore throat (2.5 visits). Although oral candidiasis was the most commonly reported ICS-induced ADE, it was perceived as requiring the least number of office visits for diagnosis and treatment (1.9 visits).

When treating an ICS-induced ADE, physicians could continue the ICS, reduce the dose of the ICS, discontinue the ICS, switch to a different ICS, or switch to a different long-term asthma controller (LTC) agent (see Figure 4). In Figure 6 (see page 587), the most common treatment strategy reported was to reduce the dose of the ICSs (for 26% to 30% of patients) or to switch to a different ICS agent (for 14% to 29% of patients). Between 18% and 21% of physicians reported that they would continue ICS therapy, and 7% to 15% would switch to a different LTC agent.

Figure 7 (see page 588) displays the treatment outcomes of each ADE assessed in the Delphi process. The physicians reported that most ICS-induced ADEs would be adequately resolved but that 14% to 29% would remain unresolved after treatment. Cough and dysphonia were most likely to remain unresolved, with approximately 29% of patients reported as still complaining of symptoms. Physicians reported that fewer than 1% to 5% of patients would have no change in symptomatology, 12% to 18% of patients would have “reduced” symptoms, and 2% to 9% of patients would require a referral visit for further treatment. The most common ADEs resulting in a referral visit were cough and dysphonia.

After the initial diagnostic visit, patients could either have no follow-up physician contact, follow-up physician office visits, or a follow-up physician telephone call to manage the ICS-induced ADE (see Figure 5). The panel reported that between 18% and 29% of patients would have no follow-up contact after the initial visit. Of the patients with follow-up physician office visits, those with dysphonia would typically need 1.6 visits, those with cough would require 1.4 visits, and those with sore throat would need one visit.

The Verispan Physician Drug and Diagnosis Audit for 2003 reported that 83.2% of patients with mild, moderate, or severe asthma received a prescription for either a single-entity or combination ICS. Applying this value to the U.S. population with asthma (20 million adults and children), approximately 16.6 million patients in the U.S. received an ICS agent.1,2 Using the frequency of ADEs determined from the Delphi panel, approximately 3.3 million patients have ICS-induced cough, oral candidiasis, dysphonia, or sore throat, and slightly more than nine million office visits take place to manage these ADEs.

The cost of a physician office visit was derived from the 2004 Physicians’ Fee and Coding Guide. The mean cost for an established non-Medicare patient with level 2 complexity of medical decision-making was $51.50.28 Table 5 lists the calculated costs for each ICS-induced ADE.

Cough was the most costly oropharyngeal ADE, at approximately $154 million, and was associated with more than 2.9 million office visits, followed by dysphonia and sore throat. Oral candidiasis was reported to be the least costly ADE.

The total cost of managing ICS-induced cough, oral candidiasis, dysphonia, and sore throat was approximately $464 million for patients with asthma in the U.S. who used an ICS. This represents a burden of $1.60 per person per year, or $0.13 per person per month, for the entire U.S. population, assuming that each patient with asthma using an ICS has only one episode of oropharyngeal ADEs that is severe enough to warrant care-seeking annually.

We conducted sensitivity analysis on the frequency of ADEs and the cost of each ADE to determine the potential cost savings associated with preventing or managing these ADEs.

In Figure 3, we validated a “seeding” algorithm for the diagnosis of adverse effects induced by inhaled corticosteroids.

Figure 3 Validated “seeding” algorithm for the diagnosis of adverse effects induced by inhaled corticosteroids.
analyses to test the robustness of the total costs to changes in the frequency of ICS-induced ADEs and the number of physician office visits required to manage the ADEs. A Monte Carlo simulation indicated that the total cost of physician office visits for ICS-induced ADEs ranged between $291 million and $642 million. Figure 8 (see page 588) shows the results of changing each of these variables independently while holding all other variables constant.

The total cost of physician office visits is most sensitive to the frequency of cough in patients using an ICS and the average number of office visits to manage cough. Oral candidiasis, although the most commonly occurring ADE, had the least influence on the total cost of physician office visits. However, even if the total number of office visits made annually for each ADE were reduced by 25%, the total cost of the visits would still be approximately $348 million. This would decrease the total number of office visits to approximately 6.8 million.

DISCUSSION

Inhaled corticosteroids are a major component of asthma treatment, both in accordance with treatment guidelines and as seen in clinical practice.8,20,30 Observational studies in the literature and clinical trials have shown that the prevalence of oropharyngeal ADEs is similar to or greater than reported in ICS package inserts and that these ADEs affect patient satisfaction and compliance with ICS therapy.13,14 Although the incidence of ADEs is known, little has been done to quantify their economic burden as related to physician office visits.

The current study was designed to determine the burden of ICS-induced ADEs in clinical practice based on physician experience. The results of the Delphi Panel process indicate that the frequency of ICS-induced ADEs may be slightly higher than reported in the literature or trials cited in package inserts but is lower than what is reported in observational studies.13,14,25 The lower rate reported might be explained by the attempt of the Delphi process to quantify only oropharyngeal ADEs severe enough to warrant care-seeking. Whereas the mean number of office visits reported for the diagnosis and treatment of the ADEs seems high, these are probably the most severe of the ADEs, because they induced care-seeking. Moreover, this is one of the first attempts to isolate patterns of care in terms of oropharyngeal ICS-induced ADEs; thus, there is little information in the literature against which to
compare these findings. Although the results of this study rely on expert survey evidence, the Delphi methodology provides a rigorous approach to obtaining information from experts in the field.

The cost to the U.S. health care system in terms of office visits is more than $464 million for patients with asthma receiving ICS therapy. From a payer perspective, this represents approximately $0.13 per person per month, assuming similar prevalence rates of asthma and the use of ICSs. With the development of new ICS therapies having potentially improved tolerability profiles, it is hoped that this burden, in both dollars and physician time, will be reduced.

In 2001, more than 27 million physician office visits were made for patients with any complaint of cough. The Delphi Panel found that approximately three million physician office visits were made for ICS-induced cough, which accounts for approximately 11% of the 27 million visits made for any complaint of cough. The projected cost of the 27 million office visits for the primary complaint of cough would be $1.4 billion; therefore, the cost of ICS-induced cough is approximately 11% of the total cost of office visits for cough ($154 million).

Only the cost of the office visit was used to calculate total costs. Therefore, the costs of ICS-induced ADEs presented here may actually be an underestimate of the total costs because they do not include medication costs (e.g., over-the-counter remedies for cough), therapy changes, diagnostic services ordered, or differential costs for specialty physician office visits (e.g., the cost of a pulmonologist visit versus the cost of a family practice visit).

Physician office visits are likely to remain a major cost driver in the total costs of ICS-induced ADEs because of the imprecise nature of oropharyngeal ADEs, particularly their vague symptomatology and diverse etiology. Cough and dysphonia, for example, can be caused by other disease states (e.g., chronic obstructive pulmonary disease and infection), patient behaviors (e.g., smoking), or other medications (e.g., angiotensin-converting enzyme inhibitors, antihistamines); moreover, the clinical presentation varies significantly from patient to patient.

In managing ICS-induced ADEs, physicians perceive oropharyngeal ADEs to be a drug class effect. Approximately 30% of patients with an ADE discontinued taking an ICS agent and were switched to either an LTC agent or a different class of controller medications. Similarly, physicians may view ADEs as dose-dependent, in that they lowered the ICS dose in almost one-third of patients presenting with an ADE.

Physicians may minimize any ICS product-specific differences and manage patients similarly, regardless of

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**Inhaled Corticosteroid–Induced Adverse Effects**

The ICS-induced XYZ Follow-up Algorithm pertains to patient contacts (office visits or phone calls) made after the presumptive diagnosis of ICS-induced XYZ has been established. The intent of the algorithm is to determine the frequency of follow-up contact specifically for ICS-induced XYZ and not for routine follow-up visits.

Please fill in the percent likelihood of each follow-up option in the algorithm. The percentages for all boxes in the same color must total 100%.

![ICS-induced XYZ Follow-up Algorithm](image-url)

Figure 5 Validated “seeding” algorithm for follow-up care related to inhaled corticosteroid (ICS)–induced adverse effects.

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*continued on page 587*
ICS agent. For example, physicians responded that they would prescribe the same ICS agent for more than 50% of patients with oral candidiasis, with or without a dose reduction, even though ICS agents have different potencies and are associated with various rates of oral candidiasis. Physicians would switch ICS agents in fewer than 15% of patients with oral candidiasis.

**STUDY LIMITATIONS**

Although this is the first such study to quantify the economic impact of oropharyngeal ADEs caused by ICS agents, several limitations should be acknowledged. Because of the construct of the Delphi process, the number of physician office visits needed to manage ICS-induced ADEs may have been overestimated. Panel members were instructed to consider a patient presenting with an ICS-induced oropharyngeal ADE but were given no directions for patients presenting with multiple complaints at one office visit. Therefore, patients with oral candidiasis caused by an ICS may also have presented with oral candidiasis–induced dysphonia and cough in one office visit rather than in three visits.

Panel members were instructed to consider only patients who were seeking care rather than patients with incidental complaints but with an unrelated primary complaint. Whether the Delphi process results represent only patients seeking care would be difficult to verify. In an effort to address this limitation, the average number of physician office visits needed to diagnose and manage an ADE was decreased to the national average number of diagnoses made during an office visit. This number was obtained from U.S. survey data that reflect physicians making several diagnoses within one office visit.

As the average number of diagnoses made during an office visit in 2003 was between 1.5 and 1.75, the associated total cost of ICS-induced ADEs decreased by 22% to 31% ($320 million to $362 million). Even with this decrease, the total costs...
still represent a significant economic impact, albeit of a slightly lesser magnitude.

Other limitations include those associated with the Delphi Panel methodology. The use of any survey is subject to potential bias in selection, reporting, and recall. The panel was composed of 15 physicians, and there may be inherent limitations in the ability to generalize these physicians’ practices to national practices.

The Delphi methodology specifically addresses many of the biases associated with survey research by requiring a consensus. However, a retrospective database analysis may eliminate other biases (such as recall bias), whereby all panel members may be skewing their results toward one memorable patient instead of the breadth of patients seen. Still, a retrospective database analysis would introduce other biases (such as selection bias), whereby patients with the most severe cases of asthma are prescribed an ICS preferentially. This may lead to the overestimation of an ADE such as cough because this ADE is related to the severity of the disease state and to the propensity to receive ICS treatment.

Conversely, a retrospective database analysis may lead to an underestimation of other ADEs that are likely to be viewed as nuisance symptoms stemming from ICS use. These symptoms may not warrant the time or effort to code according to the ICD-9 classification, and they may result in the selection of a more readily available ICD-9 code such as asthma.

The Delphi process of consensus building attempted to minimize any outlying differences by allowing panel mem-

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**Figure 7** Reported outcomes of inhaled corticosteroid–induced adverse effects. OC = oral candidiasis.

**Figure 8** Sensitivity analyses. This tornado diagram (a graphical representation of model sensitivity) depicts the variables most influential on the total cost of physician office visits. Holding all other variables constant, each variable is changeable around the mean value between the ranges to the far left and right of each row. On the basis of this variance, the average total cost of office visits, in U.S. millions of dollars, can be read from the y-axis. OV = office visit.
bers to review the panel’s responses and reassess their own responses. The prevalence of asthma has probably increased in recent years since the last published National Health Interview Survey, so the underestimated prevalence of asthma may result in an underestimate of the current costs of ICS-induced ADEs. In this study, we did not account for differences in treatment resulting from the diverse patient population.

Because the Delphi process relies on expert survey evidence, there may be some variance in the reproducibility of the results. Although other study designs could have been used, we felt that the Delphi process would provide a feasible, preliminary estimation of the burden of ICS-induced ADEs. An intermediate step could be conducted prior to prospective research (e.g., performing a retrospective claims analysis by using a control group to determine the attributable risk of office visits in patients using an ICS); however, further research using a chart audit or prospective studies should still be conducted to validate these initial findings. Such prospective work would minimize any potential bias associated with recall or reporting by following a case of ICS-induced ADE as it actually occurs rather than as a hypothetical situation.

CONCLUSION

The overall economic burden of ICS-induced oropharyngeal ADEs can be significant. Often overlooked as unavoidable consequences of asthma therapy, these ADEs are a major source of health care resource utilization, especially physician services. Novel and more tolerable ICS agents with a reduced risk of ADEs have the potential to decrease the overall number of physician office visits. In light of the research discussed here, oropharyngeal ADEs and potential differences in rates of these ADEs among ICS products require more attention during P&T committee reviews of the ICS class.

Given the substantial use of resources for ICS-induced ADEs, any potential differences among agents in the rate of ADEs warrant consideration. To validate the results found in this study, however, we need further prospective studies. Similarly, future research should assess differences in the rates of care-seeking and treatment patterns among ICS agents attributable to oropharyngeal ADEs. Such research may be helpful in determining strategies for decreasing the economic impact of these common ADEs.

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