

## Treatment of Allergic Rhinitis: An Evidence-Based Evaluation of Nasal Corticosteroids Versus Nonsedating Antihistamines

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### **Abstract**

Allergic rhinitis is a high-cost, high-prevalence disease. In the 12 months ending March 31, 1997 \$3.1 billion was spent in the United States for medications to manage this illness. Allergic rhinitis affects quality of life and interferes with work productivity. Nonsedating antihistamines are the most common and most expensive therapy for this condition. This study reviewed 13 randomized studies in which blinded investigators compared management of allergic rhinitis by means of intranasal steroids to management by means of nonsedating antihistamine. Evidence tables demonstrated that in all studies in which total nasal symptoms and nasal obstruction were recorded, the nasal steroid was statistically superior to the nonsedating antihistamine. For nasal blockage the nonsedating antihistamines did not perform better than placebo. For all other nasal symptoms the intranasal steroid was statistically superior in most reports and equal or numerically better in the remaining papers. When these data are linked to those from cost analysis and quality-of-life studies, the evidence strongly suggests that nasal steroids should be first-line therapy for allergic rhinitis. In four reports on the combination of a nonsedating antihistamine compared to a nasal steroid alone, there was no significant difference between these two treatments. Like asthma, allergic rhinitis is an inflammatory disease and should be managed with anti-inflammatory medication. Making such a change in the management of allergic rhinitis should increase efficacy and decrease costs.

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Allergic rhinitis is a high-cost, high-prevalence disease. The 1-year prevalence is estimated at 7.5% to 8.2%<sup>1</sup> with lifetime prevalence at more than 20% among the population of the United States. In a study in London, England, the period prevalence of all forms of rhinitis was 24%; 63% of the cohort were considered to have atopy with nasal blockage as the most common principal symptom.<sup>2</sup> In the United States the cost of medication to manage rhinitis for the 12 months ending March 31, 1997, was \$3.1 billion; 77% of this amount was spent on prescription pharmaceuticals. More money was spent on prescription medication for allergic rhinitis than for asthma. Nonsedating antihistamines accounted for \$1.6 billion (42.5 million prescriptions) and nasal steroids for \$0.8 billion (22.5 million prescriptions) (Scott-Levin [Plymouth Meeting, PA] and IMS [Newtown, PA] sales data, 1997).

Prescribing patterns confirm that nonsedating antihistamines are frequently used as primary therapy for allergic rhinitis. Primary care<sup>3,4</sup> and allergy textbooks either recommend antihistamines as first-line therapy or make no suggestion about order of care. *Cecil Textbook of Medicine* states, "If avoiding allergens does not result in improvement, antihistamine therapy is a reasonable next step."<sup>3</sup> In discussions of treatment options, recommendations should be based on evidence from well-designed clinical trials in which subjects are randomly assigned and the investigators are blinded. Recommendation should not be based solely on reasonable clinical impression.

Malone et al estimated the cost of treating patients with allergic rhinitis at \$0.8 billion to \$1.48 billion per year for 1994.<sup>5</sup> This estimate is low considering that the cost of medication alone exceeds this figure. Loss of productivity due to allergic rhinitis is high,<sup>6</sup> and this loss may be magnified when first-generation antihistamines are used.<sup>7</sup> Other studies have demonstrated the negative effect of allergic rhinitis on health-related quality of life.<sup>8</sup> These data demonstrate the importance of studying this illness. We present evidence

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tables of the comparative literature on the management of allergic rhinitis.

... METHODS ...

A Medline search was conducted to cover the years 1976 to March 1997. Articles were included in this review if they contained terms related to both an inhaled nasal steroid (beclomethasone, budesonide, fluticasone, flunisolide, mometasone, or triamcinolone) and a non-sedating antihistamine (astemizole, cetirizine, fexofenadine, loratadine, or terfenadine). Seventeen published and peer-reviewed studies were found with this search. Abstracts of recent research were also considered for inclusion in this review if the study was a randomized, double-blinded one that compared use of an intranasal steroid with use of a non-sedating antihistamine. Using this criteria, two published abstracts also were included in the analysis.<sup>22,26</sup>

Of the 19 initial studies, six were excluded from analysis because one was an open-labeled study,<sup>9</sup> one was a cross-over study,<sup>10</sup> two included use of combination products,<sup>11,12</sup> one was an antigen challenge and not a study of symptoms,<sup>13</sup> and one presented no numerical data for interpretation.<sup>14</sup>

Bernstein et al,<sup>15</sup> Bunnag et al,<sup>16</sup> Darnell et al,<sup>17</sup> Frølund,<sup>18</sup> Jordana et al,<sup>19</sup> Juniper et al,<sup>20</sup> Salomonsson et al,<sup>21</sup> Schenkel et al,<sup>22</sup> Schoenwetter and Lim,<sup>23</sup> and Simpson<sup>24</sup> used a four-point scale to grade symptoms (0 = none, 1 = mild, 2 = moderate, 3 = severe). Bronsky et al,<sup>25</sup> Ratner et al,<sup>26</sup> and van Bavel et al<sup>27</sup> used an analog scale from 0 to 100 (0 = absent to 100 = severe). To allow comparison of the results from the latter three studies with those from the other studies, the data

from the studies by Bronsky et al, Ratner et al, and van Bavel et al were normalized to the four-point scale by means of division by 25. The corresponding *P* values are unchanged with this scale adjustment. Darnell et al<sup>17</sup> used a four-point scale that varied with each symptom but correlated with absent to severe symptoms. *P* values from eight of the 13 studies were based on mean differences. In four studies<sup>16,17,21,24</sup> investigators used categorical or nonparametric procedures to evaluate differences in treatment group results. Although not comparable with a *P* value in the other eight studies, the results were assessed to determine whether the results were consistent with the combined *P* value.

Symptoms evaluated were not the same across all studies. For this analysis, total symptom score, itchy nose, stuffy nose (congestion or blockage), runny nose, and sneezing were the main outcome parameters evaluated. Results were included if there were numerical data or graphs from which the results could be extrapolated for statistical analysis. Ocular symptoms were evaluated in several studies, but the findings reported varied and could not be combined. In four studies investigators evaluated the effect of nasal steroids and non-sedating antihistamines alone and in combination.

... RESULTS ...

Table 1 summarizes the results. For total nasal symptoms and stuffy nose the intranasal steroid sprays were superior to the non-sedating antihistamines in all studies, a statistically significant finding. Other nasal symptoms were best managed with nasal steroids in most of the studies. Non-sedating antihistamines were never statistically superior to the nasal steroids in any of the studies for any nasal parameter investigated.

Total nasal symptom scores are reported in Table 2. Regardless of the length of treatment, nasal corticosteroids were statistically superior to non-sedating antihistamines in all studies in which this outcome measure was reported. In all of the 12 studies in which nasal congestion was evaluated (Table 3), nasal steroids were more efficacious than non-sedating

**Table 1.** Summary of Studies

| Parameter      | Treatment     | N   | Change from Baseline | Total No. of Studies | Studies with <i>P</i> < 0.05 Favoring Nasal Steroids |
|----------------|---------------|-----|----------------------|----------------------|------------------------------------------------------|
| Total Symptoms | Nasal steroid | 741 | -5.4                 | 8                    | 8/8 (100%)                                           |
|                | Antihistamine | 752 | -3.3                 |                      |                                                      |
| Stuffy Nose    | Nasal steroid | 598 | -1.1                 | 12                   | 12/12 (100%)                                         |
|                | Antihistamine | 598 | -0.6                 |                      |                                                      |
| Itchy Nose     | Nasal steroid | 568 | -1.4                 | 9                    | 6/9 (67%)                                            |
|                | Antihistamine | 568 | -0.8                 |                      |                                                      |
| Runny Nose     | Nasal steroid | 598 | -1.2                 | 11                   | 8/11 (73%)                                           |
|                | Antihistamine | 598 | -0.6                 |                      |                                                      |
| Sneezing       | Nasal steroid | 598 | -1.1                 | 11                   | 8/11 (73%)                                           |
|                | Antihistamine | 598 | -0.7                 |                      |                                                      |

antihistamines, a statistically significant finding. In five of the studies,<sup>17,24-27</sup> nonsedating antihistamine was compared with placebo in the management of congestion. In all of these comparisons the effect of the use of a nonsedating antihistamine could not be differentiated from that of placebo treatment.

Nasal itching was evaluated in nine studies (Table 4). Use of nasal corticosteroids was statistically superior in six studies. In two studies that did not show a statistically significant difference, the numerical differences favored nasal corticosteroids. One study showed no difference between therapies. Eleven studies presented results for runny nose (Table 5). In eight studies the effect of use of nasal steroids was statistically superior, and in the other three the results favored use of nasal steroids. In the studies by Bernstein et al<sup>15</sup> and Bunnag et al,<sup>16</sup> statistically significant differences favored use of nasal steroids at week 2 but not at the end of the study. These two studies were included with the three studies that favored use of nasal steroids. When sneezing was evaluated as a symptom, eight of the 11

studies statistically favored use of nasal steroids. In the study by Darnell et al<sup>17</sup> the differences approached statistical significance (Table 6).

Eye symptoms were recorded inconsistently in the studies. Ocular symptom data were collected in 10 of the 13 studies. Only in the study by Frølund were there statistically significant differences for total eye symptoms in favor of nonsedating antihistamines (the sum of redness, itching, and tearing). No other study in which eye symptoms were evaluated singly or in combination showed any statistically significant differences.

Four studies compared a nasal steroid alone and the combination of the nasal steroid and the antihistamine.<sup>20,22,24,26</sup> Schenkel et al<sup>22</sup> reported only total nasal symptoms and total combined symptoms. There were no statistically significant differences between the two groups. In the three studies in which specific nasal symptoms were evaluated, the data for the combination of the two medications could not be differentiated from data on nasal steroid spray alone, with the exception of sneezing in the study by Simpson.<sup>24</sup> This parameter favored the combination.

**Table 2.** Total Nasal Symptoms

| Reference                          | Treatment      | Treatment Length (Weeks) | No. of Patients | Baseline Score | Change | P Value* |
|------------------------------------|----------------|--------------------------|-----------------|----------------|--------|----------|
| Bernstein et al <sup>15</sup>      | Triamcinolone  | 4                        | 104             | 9.10           | -4.55  | ≤0.05    |
|                                    | Astemizole     |                          | 105             | 9.07           | -3.36  |          |
| Bronsky et al <sup>25</sup>        | Fluticasone    | 4                        | 117             | 10.84          | -6.32  | ≤0.05    |
|                                    | Loratadine     |                          | 116             | 11.16          | -4.32  |          |
| Frølund <sup>18</sup>              | Beclomethasone | 2                        | 30              | 7.9            | -4.00  | ≤0.05    |
|                                    | Astemizole     |                          | 30              | 8.1            | -2.40  |          |
| Ratner et al <sup>26</sup>         | Fluticasone    | 2                        | 150             | 11.60          | -6.80  | ≤0.001   |
|                                    | Loratadine     |                          | 150             | 11.60          | -2.80  |          |
| Salomonsson et al <sup>21</sup>    | Beclomethasone | 4                        | 77              | NA             | NA     | <0.05    |
|                                    | Astemizole     |                          | 80              | NA             | NA     |          |
| Schenkel et al <sup>22</sup>       | Mometasone     | 2                        | 176             | NA             | -4.9   | ≤0.01    |
|                                    | Loratadine     |                          | 181             | NA             |        |          |
| Schoenwetter and Lim <sup>23</sup> | Triamcinolone  | 4                        | 134             | 9.90           | -5.80  | ≤0.01    |
|                                    | Loratadine     |                          | 140             | 9.50           | -3.30  |          |
| van Bavel et al <sup>27</sup>      | Fluticasone    | 2                        | 78              | NA             | NA     | ≤0.05    |
|                                    | Terfenadine    |                          | 77              | NA             | NA     |          |

\*Statistical differences favor nasal steroids  
NA = Not available.

... DISCUSSION ...

The evidence tables demonstrate the superiority of nasal steroids over nonsedating antihistamines in the treatment of patients with allergic rhinitis. Total symptom scores always favored the nasal corticosteroid. Relief of nasal blockage, the principal symptom of most patients, was universally superior with use of nasal steroids, and the nonsedating antihistamine fared no better than placebo for this parameter. All other symptom scores favored the nasal steroid in most of the studies. In the few studies in which there were no statistical differences, the numerical differences favored nasal steroids.

For each of the study parameters, there were approximately 1800 subjects. Fluticasone propionate

was the most studied nasal corticosteroid, and the power of the conclusions may be weighted by the results from these investigations. Eight more abstracts have been presented that demonstrate the superiority of fluticasone propionate compared with nonsedating antihistamines (loratadine four studies; astemizole, three studies; cetirizine, one study). These studies are summarized in the review by Wiseman and Benfield.<sup>28</sup> Sufficient data were not available to allow inclusion of these studies in the evidence tables, but the abstracts indicate the trend for superiority of nasal steroids. Two abstracts from the annual national allergy meetings are represented in the evidence tables. Exclusion of these data would not have altered the statistical significance of the results. Expanding the database in evidence tables when the information is

**Table 3.** Nasal Symptom: Stuffy Nose (Obstruction or Blockage)

| Reference                          | Treatment      | Treatment Length (Weeks) | No. of Patients | Baseline Score | Change | P Value* |
|------------------------------------|----------------|--------------------------|-----------------|----------------|--------|----------|
| Bernstein et al <sup>15</sup>      | Triamcinolone  | 4                        | 104             | 1.93           | -0.84  | ≤0.05    |
|                                    | Astemizole     |                          | 105             | 2.00           | -0.53  |          |
| Bronsky et al <sup>25</sup>        | Fluticasone    | 4                        | 117             | 2.84           | -1.44  | ≤0.05    |
|                                    | Terfenadine    |                          | 116             | 2.96           | -0.96  |          |
| Bunnag et al <sup>16</sup>         | Budesonide     | 4                        | 33              | 1.64           | -0.93  | 0.01     |
|                                    | Astemizole     |                          | 34              | 1.14           | -0.14  |          |
| Darnell et al <sup>17</sup>        | Fluticasone    | 6                        | 67              | NA             | NA     | 0.018    |
|                                    | Terfenadine    |                          | 72              | NA             | NA     |          |
| Frølund <sup>18</sup>              | Beclomethasone | 2                        | 30              | NA             | NA     | <0.05    |
|                                    | Loratadine     |                          | 30              | NA             | NA     |          |
| Jordana et al <sup>19</sup>        | Fluticasone    | 4                        | 121             | NA             | NA     | <0.001   |
|                                    | Loratadine     |                          | 119             | NA             | NA     |          |
| Juniper et al <sup>20</sup>        | Beclomethasone | 6                        | 30              | 0.41           | -0.02  | <0.05    |
|                                    | Astemizole     |                          | 30              | 0.25           | 0.06   |          |
| Ratner et al <sup>26</sup>         | Fluticasone    | 2                        | 150             | 3.12           | -1.60  | <0.008   |
|                                    | Loratadine     |                          | 150             | 3.12           | -0.64  |          |
| Salomonsson et al <sup>21</sup>    | Beclomethasone | 4                        | 77              | NA             | NA     | <0.05    |
|                                    | Astemizole     |                          | 80              | NA             | NA     |          |
| Schoenwetter and Lim <sup>23</sup> | Triamcinolone  | 4                        | 134             | 2.10           | -0.90  | <0.001   |
|                                    | Loratadine     |                          | 140             | 2.10           | -0.50  |          |
| Simpson <sup>24</sup>              | Budesonide     | 3                        | 30              | NA             | NA     | 0.05     |
|                                    |                |                          | 23              | NA             | NA     |          |
| van Bavel et al <sup>27</sup>      | Fluticasone    | 2                        | 78              | NA             | NA     | ≤0.05    |
|                                    | Terfenadine    |                          | 77              | NA             | NA     |          |

\*Statistical differences favor nasal steroids.  
NA = Not available.

available is important because negative findings frequently are not reported.

We could find only one published study that compared use of an antihistamine-decongestant preparation with use of an intranasal steroid.<sup>12</sup> This study did not demonstrate any statistical differences between the results with the two drugs. Addition of the systemic decongestant did add to the adverse effects of the drug, including insomnia and nervousness.<sup>25</sup> These combination products are typically more expensive than nasal steroid sprays.

Adverse effects of the medications may motivate providers to prescribe one class of medication over another. In these clinical trials the frequency of side effects was low and was comparable in both treatment groups. Local irritation and epistaxis are the most common side effects of use of nasal steroids. Candidiasis, decrease in linear growth of children, and osteoporosis have not been reported with the use of intranasal steroids.<sup>29</sup>

Ross found that loss of productivity due to use of first-generation antihistamines in the management of

allergic rhinitis may cost as much as \$3.8 billion dollars a year.<sup>7</sup> Nasal steroids, because they provide freedom from sedative effects and are clinically more effective, may help improve productivity. Bowers et al<sup>30</sup> demonstrated that fluticasone propionate is associated with less interference at work from the effects of seasonal allergic rhinitis than is loratadine. Gilmore et al reported that both antihistamines (predominantly first generation) and antibiotics, not antidepressants, anti-anxiety medication, or narcotics, were associated with an increased odds ratio of on-the-job injury.<sup>31</sup> This suggests that it may be the illness and not the treatment that puts workers at risk. These studies indicate that the ideal therapy for allergic rhinitis should both decrease the number of workdays lost due to illness and be free from adverse effects. Nasal steroids have these two attributes.

The evidence from these clinical studies supports the use of nasal steroids as first-line therapy for allergic rhinitis. Clinically they are more effective medications, and from a cost perspective they are 30% less expensive per treatment month. The average wholesale price of

**Table 4.** Nasal Symptom: Itchy Nose

| Reference                          | Treatment     | Treatment Length (Weeks) | No. of Patients | Baseline Score | Change | P Value* |
|------------------------------------|---------------|--------------------------|-----------------|----------------|--------|----------|
| Bernstein et al <sup>15</sup>      | Triamcinolone | 4                        | 104             | 1.85           | -1.00  | <0.05    |
|                                    | Astemizole    |                          | 105             | 1.75           | -0.74  |          |
| Bronsky et al <sup>25</sup>        | Fluticasone   | 4                        | 117             | 2.68           | -1.64  | ≤0.05    |
|                                    | Terfenadine   |                          | 116             | 2.76           | -1.04  |          |
| Bunnag et al <sup>16</sup>         | Budesonide    | 4                        | 33              | 1.00           | -0.79  | 0.34     |
|                                    | Astemizole    |                          | 34              | 0.57           | -0.50  |          |
| Darnell et al <sup>17</sup>        | Fluticasone   | 6                        | 67              | NA             | NA     | NS       |
|                                    | Terfenadine   |                          | 72              | NA             | NA     |          |
| Jordana et al <sup>19</sup>        | Fluticasone   | 4                        | 121             | NA             | NA     | ≤0.011   |
|                                    | Loratadine    |                          | 119             | NA             | NA     |          |
| Ratner et al <sup>26</sup>         | Fluticasone   | 2                        | 150             | 3.04           | -1.52  | ≤0.008   |
|                                    | Loratadine    |                          | 150             | 3.04           | -0.80  |          |
| Schoenwetter and Lim <sup>23</sup> | Triamcinolone | 4                        | 134             | 1.85           | -1.65  | ≤0.001   |
|                                    | Loratadine    |                          | 140             | 2.00           | -0.85  |          |
| Simpson <sup>24</sup>              | Budesonide    | 3                        | 30              | NA             | NA     | NS       |
|                                    | Terfenadine   |                          | 23              | NA             | NA     |          |
| van Bavel et al <sup>27</sup>      | Fluticasone   | 2                        | 78              | NA             | NA     | ≤0.05    |
|                                    | Terfenadine   |                          | 77              | NA             | NA     |          |

\*Statistical differences favor nasal steroids.  
NA = Not available; NS = Not significant.

fluticasone propionate is approximately \$38 per month, for loratadine approximately \$65 dollars per month, and the combination is \$90 per month. Results of cost-effectiveness analysis favor the use of fluticasone over both loratadine and terfenadine.<sup>32</sup> Results of quality-of-life studies<sup>33</sup> also favor use of an intranasal steroid. All of the measurable outcome parameters presented favor the use of intranasal steroids. The sales figures for these two product classes demonstrate that the choice is being made on the basis of clinical impression not evidence.

Fear of the use of steroids, on the part of either provider or patient, may be one explanation for the trend in prescribing that favors nonsedating antihistamines. Another reason is that it is simpler for providers to administer a pill or liquid than to instruct patients in how to use a nasal steroid spray. Compliance with oral forms of medications also may

be better. Faster onset of action of one drug class may be another reason, but no comparative studies have evaluated this parameter. Antihistamines reach clinical effectiveness within 5 to 7 hours of administration.<sup>29</sup> The package insert for intranasal fluticasone reads that improvement may start in 12 hours, and the insert for triamcinolone that improvement may be seen within the first day of use. The onset of action of nasal steroids appears to occur sooner than previously thought<sup>15</sup> (Flonase package insert, Glaxo Wellcome, Research Triangle Park, NC, 1997).

It has been suggested that patients with severe symptoms use nasal steroids and nonsedating antihistamines in combination.<sup>34</sup> Clinical trials of dual therapy do not support this recommendation. The finding that use of nasal steroids is as effective as combination treatment suggests that this approach should be the

**Table 5.** Nasal Symptom: Runny Nose (Rhinorrhea)

| Reference                          | Treatment      | Treatment Length (Weeks) | No. of Patients | Baseline Score | Change | P Value*        |
|------------------------------------|----------------|--------------------------|-----------------|----------------|--------|-----------------|
| Bernstein et al <sup>15</sup>      | Triamcinolone  | 4                        | 104             | 1.73           | -0.89  | NS <sup>†</sup> |
|                                    | Astemizole     |                          | 105             | 1.79           | -0.70  |                 |
| Bronsky et al <sup>25</sup>        | Fluticasone    | 4                        | 117             | 2.84           | -1.68  | <0.05           |
|                                    | Terfenadine    |                          | 116             | 2.84           | -1.16  |                 |
| Bunnag et al <sup>16</sup>         | Budesonide     | 4                        | 33              | 1.00           | -0.86  | 0.29*           |
|                                    | Astemizole     |                          | 34              | 1.07           | -0.57  |                 |
| Darnell et al <sup>17</sup>        | Fluticasone    | 6                        | 67              | NA             | NA     | 0.027           |
|                                    | Terfenadine    |                          | 72              | NA             | NA     |                 |
| Jordana et al <sup>19</sup>        | Fluticasone    | 4                        | 121             | NA             | NA     | <0.001          |
|                                    | Loratadine     |                          | 119             | NA             | NA     |                 |
| Juniper et al <sup>20</sup>        | Beclomethasone | 6                        | 30              | 0.28           | 0.03   | ≤0.05           |
|                                    | Astemizole     |                          | 30              | 0.07           | 0.04   |                 |
| Ratner et al <sup>26</sup>         | Fluticasone    | 2                        | 150             | 3.12           | -1.32  | <0.008          |
|                                    | Loratadine     |                          | 150             | 3.12           | -0.64  |                 |
| Salomonsson et al <sup>21</sup>    | Beclomethasone | 4                        | 77              | NA             | NA     | <0.05           |
|                                    | Astemizole     |                          | 80              | NA             | NA     |                 |
| Schoenwetter and Lim <sup>23</sup> | Triamcinolone  | 4                        | 134             | 2.00           | -1.10  | ≤0.001          |
|                                    | Loratadine     |                          | 140             | 1.80           | -0.50  |                 |
| Simpson <sup>24</sup>              | Budesonide     | 3                        | 30              | NA             | NA     | NS              |
|                                    | Terfenadine    |                          | 23              | NA             | NA     |                 |
| van Bavel et al <sup>27</sup>      | Fluticasone    | 2                        | 78              | NA             | NA     | ≤0.05           |
|                                    | Terfenadine    |                          | 77              | NA             | NA     |                 |

\*Statistical differences favor nasal steroids.

†Significantly different at week 2 ( $P \leq 0.001$ ).

NA = Not available; NS = Not significant

exception rather than the standard of practice until there is evidence to the contrary. Combined therapy more than doubles the cost of treatment without meaningful evidence of additional benefit.

... CONCLUSION ...

Allergic rhinitis is an inflammatory disease. The evidence tables indicate that this condition is best managed with anti-inflammatory medication. In the decade since asthma has been recognized as an inflammatory disease, the treatment of patients with asthma has evolved from therapy with bronchodilators to the recommendation that anti-inflammatory agents be used as first-line therapy. The National Institutes of Health suggest that patients who need bronchodilators more than twice a week start anti-inflammatory therapy.<sup>35</sup> The same shift in the management of allergic rhinitis is supported by our evidence-table analysis.

In the recent series on quality in the *New England Journal of Medicine*, Berwick suggested that capitated managed healthcare with the appropriate use of advanced information systems can both improve health outcomes and reduce the total cost of care.<sup>36</sup> The evidence tables herein demonstrate how this concept can be applied. Clinical decisions should be based on a review of the relevant evidence from the literature, patient-oriented outcomes, and the effect on both direct and indirect costs. The evidence favors use of intranasal steroids in the treatment of patients with allergic rhinitis.

... REFERENCES ...

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**Table 6.** Nasal Symptom: Sneezing

| Reference                          | Treatment      | Treatment Length (Weeks) | No. of Patients | Baseline Score | Change | P Value* |
|------------------------------------|----------------|--------------------------|-----------------|----------------|--------|----------|
| Bernstein et al <sup>15</sup>      | Triamcinolone  | 4                        | 104             | 1.88           | -1.04  | <0.05    |
|                                    | Astemizole     |                          | 105             | 1.90           | -0.81  |          |
| Bronsky et al <sup>25</sup>        | Fluticasone    | 4                        | 117             | 2.48           | -1.56  | <0.05    |
|                                    | Terfenadine    |                          | 116             | 2.60           | -1.04  |          |
| Bunnag et al <sup>16</sup>         | Budesonide     | 4                        | 33              | 1.00           | -0.79  | 0.20     |
|                                    | Astemizole     |                          | 34              | 1.14           | -0.57  |          |
| Darnell et al <sup>17</sup>        | Fluticasone    | 6                        | 67              | NA             | NA     | 0.057    |
|                                    | Terfenadine    |                          | 72              | NA             | NA     |          |
| Jordana et al <sup>19</sup>        | Fluticasone    | 4                        | 121             | NA             | NA     | <0.01    |
|                                    | Loratadine     |                          | 119             | NA             | NA     |          |
| Juniper et al <sup>20</sup>        | Beclomethasone | 6                        | 30              | 0.32           | -0.03  | ≤0.05    |
|                                    | Astemizole     |                          | 30              | 0.14           | -0.02  |          |
| Ratner et al <sup>26</sup>         | Fluticasone    | 2                        | 150             | 2.56           | -1.04  | ≤0.008   |
|                                    | Loratadine     |                          | 150             | 2.56           | -0.52  |          |
| Salomonsson et al <sup>21</sup>    | Beclomethasone | 4                        | 77              | NA             | NA     | <0.05    |
|                                    | Astemizole     |                          | 80              | NA             | NA     |          |
| Schoenwetter and Lim <sup>23</sup> | Triamcinolone  | 4                        | 134             | 1.85           | -1.25  | ≤0.001   |
|                                    | Loratadine     |                          | 140             | 1.85           | -0.65  |          |
| Simpson <sup>24</sup>              | Budesonide     | 3                        | 30              | NA             | NA     | NS       |
|                                    | Terfenadine    |                          | 23              | NA             | NA     |          |
| van Bavel et al <sup>27</sup>      | Fluticasone    | 2                        | 78              | NA             | NA     | ≤0.05    |
|                                    | Terfenadine    |                          | 77              | NA             | NA     |          |

\*Statistical differences favor nasal steroids  
NA = Not available; NS = Not significant

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