Evaluating the cost-effectiveness of anterior uveitis investigation by Canadian ophthalmologists

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ABSTRACT • RÉSUMÉ

Background: To evaluate the cost-effectiveness of anterior uveitis investigation by Canadian ophthalmologists and to assess the role of implementing national clinical guidelines for such investigation.

Methods: Based on data extracted from the Canadian National Uveitis Survey (CNUS, 2007 version), the cost of investigating a patient with anterior uveitis, according to current practice patterns of Canadian ophthalmologists, was determined and grouped across 4 clinical scenarios: (i) nongranulomatous anterior uveitis in an adult, (ii) granulomatous anterior uveitis in an adult, (iii) granulomatous anterior uveitis with suspected sarcoidosis in an adult or a child, and (iv) nongranulomatous anterior uveitis in a child. Similarly, the cost of investigating a patient with anterior uveitis as per published evidence-based guidelines was determined and compared with the current practice pattern using a cost-minimization model, sensitivity analyses, and Monte Carlo simulations.

Results: Ophthalmologists were found to consistently order more tests than recommended by evidence-based guidelines, across each of the scenarios studied (p < 0.05). Overall, complete blood count, erythrocyte sedimentation rate, C-reactive protein, antinuclear antibody, and rheumatoid factor were the most commonly ordered extraneous tests that were not included in the evidence-based guidelines for the routine investigation of anterior uveitis. Also, there were significant differences in the cost of investigating a patient with anterior uveitis when compared with those predicted by adhering to evidence-based clinical practice guidelines. Cost minimization and sensitivity analyses revealed that published guidelines imparted cost savings when compared with current practice patterns across the 4 clinical scenarios studied (p < 0.01). The maximum additional cost was associated with investigating nongranulomatous anterior uveitis in an adult, where a minimal additional cost of $75 per patient was spent. For granulomatous anterior uveitis in an adult, the additional cost was approximately $40, whereas the additional cost for investigating an adult or a child with suspected sarcoidosis was $36. Only $11 of additional cost was spent in the workup of a child with nongranulomatous anterior uveitis. When applied to the Canadian population, adherence to the Clinical Practice Guidelines recommended by the CNUS may result in cost savings of $600,000 per year to the Canadian health care system.

Interpretation: Adherence to the evidence-based Clinical Practice Guidelines recommended by the CNUS may result in significant cost savings, with virtually no loss of sensitivity in the routine investigation of anterior uveitis in Canada.


Méthodes : Le coût de l’examen d’un patient atteint d’uvéite antérieure, selon la pratique courante des ophtalmologistes canadiens, a été établi à partir des données de l’Étude nationale canadienne sur l’uvéite (Canadian National Uveitis Survey, CNUS, version 2007) et réparti entre 4 scénarios cliniques : (i) l’uvéite antérieure non granulomateuse chez l’adulte; (ii) l’uvéite antérieure granulomateuse chez l’adulte; (iii) l’uvéite antérieure granulomateuse avec soupçon de sarcoidose chez l’adulte ou l’enfant; (iv) l’uvéite antérieure non granulomateuse chez l’enfant. De même, le coût de l’examen d’un patient atteint d’uvéite antérieure selon les lignes directrices factuelles publiées a été établi et comparé avec les modes de pratique courante compte tenu d’un modèle de minimisation du coût, des analyses de sensibilité et des simulations Monte Carlo.

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Published to guide the investigation of anterior uveitis in routine clinical practice, which was defined a priori as the one that minimized costs and had the lowest cost is considered preferred. For the analysis, we assumed that the 2 diagnostic strategies (the CNUS evidence-based guidelines and the current practice of Canadian ophthalmologists) were equivalent with respect to the clinical effectiveness of diagnosing anterior uveitis. Therefore, our econometric model compared the cost associated with the 2 diagnostic strategies to determine the preferred strategy, which was defined a priori as the one that was associated with significant cost reductions. Because of the uncertainty that exists in the baseline data, including the cost estimations, sensitivity analyses were performed.

**Methods**

The CNUS was a national survey distributed to Canadian ophthalmologists in 2004 that studied the practice patterns of 498 ophthalmologists in the routine investigation of anterior uveitis. Data regarding investigation patterns were extracted from this survey and analyzed further. All statistical and economic analyses were performed using the medical decision analysis software TreeAge, v. 3.5 (TreeAge Software, Williamstown, Mass.).

A cost-minimization model was created for a hypothetical patient with a first presentation of anterior uveitis to a Canadian Journal of Ophthalmology by Lachaine et al. compared the cost-effectiveness of prostaglandin analogues with other antiglaucoma medications for the treatment of ocular hypertension, and offered important and pragmatic recommendations for the appropriate cost-effective treatment of ocular hypertension in Canada.

In the present study, we sought to determine the potential cost savings of adherence to the CNUS Clinical Practice Guidelines in comparison with current practice patterns using a cost-minimization model. A cost-minimization analysis is a type of economic evaluation in which the effectiveness of the options under consideration is considered equivalent and therefore the option with the lowest cost is considered preferred. For the analysis, we assumed that the 2 diagnostic strategies (the CNUS evidence-based guidelines and the current practice of Canadian ophthalmologists) were equivalent with respect to the clinical effectiveness of diagnosing anterior uveitis. Therefore, our econometric model compared the cost associated with the 2 diagnostic strategies to determine the preferred strategy, which was defined a priori as the one that was associated with significant cost reductions. Because of the uncertainty that exists in the baseline data, including the cost estimations, sensitivity analyses were performed.
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Canadian ophthalmologist. Four different clinical scenarios were used: (i) moderate/severe, recurrent, chronic, or bilateral nongranulomatous anterior uveitis in an adult; (ii) anterior uveitis with granulomatous features in an adult; (iii) anterior uveitis with clinical suspicion of sarcoidosis in an adult or a child; and (iv) nongranulomatous uveitis in a child (Table 1). These clinical scenarios were formulated based on questions asked in the CNUS. Our model considers the initial workup of these patients.

An economic model was created based on 3 pieces of data: (i) the current Canadian practice patterns for the initial workup of anterior uveitis, (ii) the recommended evidence-based practice patterns for the initial workup of anterior uveitis, and (iii) the costs associated with each potential test ordered as part of the diagnostic workup under these 2 diagnostic strategies. The economic model follows the estimated practice patterns of an average Canadian ophthalmologist, which are based directly on data from the CNUS (Table 2). We calculated exact 95% confidence intervals of these estimates based on a binomial distribution.

The cost of a diagnostic workup using the guidelines recommended in the CNUS (Table 1) was compared with the cost of the current practice patterns in Canada. Cost data were obtained from a variety of sources, including the Ontario Ministry of Health schedule of benefits, the Hospitals In-Common Laboratory, and various Ontario hospital laboratories (Table 2). When a discrepancy existed among these 3 sources, the average cost of the investigation was used in the calculations. We only included variable incremental costs in our models because our analysis was based on the initial workup of patients and further downstream costs were assumed to be equivalent in the 2 arms. Indirect costs were also not included, given the aforementioned equivalence assumption. The metric used to determine the cost minimization was the Canadian dollar (valued at September 1, 2006).

**The cost-minimization model**

In order to determine potential cost savings, the costs and probabilities that various tests would be ordered were entered into the medical decision analysis program. The model was organized such that a hypothetical patient would receive a diagnostic test according to probabilities based on current Canadian practice patterns. The 2 “alternatives” in the model were diagnostic testing according to current Canadian practice patterns or according to evidence-based guidelines.

**Sensitivity analyses**

Sensitivity analyses were performed to determine our confidence in the econometric models given the inherent variability of the estimates of cost and practice patterns. For all models, a multivariate sensitivity analysis was performed in which the probabilities of diagnostic tests being ordered as part of current practice were varied over the entire range of their 95% confidence intervals simultaneously. Because costs were generally taken from 1 source and did not have an associated confidence interval, we varied costs by ±10% of baseline in our sensitivity analyses; every cost in the model was varied within this range simul-

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**Table 2—Current practice patterns in Canada based on the Canadian National Uveitis Survey**

<table>
<thead>
<tr>
<th>Test</th>
<th>Nongranulomatous, adult</th>
<th>Granulomatous, adult</th>
<th>Suspected sarcoidosis, adult or child</th>
<th>Anterior uveitis, child</th>
<th>Cost (Can$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
<td>65.1 (60.7–69.2)</td>
<td>70.5 (66.2–74.4)</td>
<td>46.2 (41.7–50.7)</td>
<td>49.8 (45.3–54.2)</td>
<td>23.79</td>
</tr>
<tr>
<td>ESR</td>
<td>51.2 (46.7–55.7)</td>
<td>55.4 (50.9–59.8)</td>
<td>—</td>
<td>36.0 (33.7–42.3)</td>
<td>1.55</td>
</tr>
<tr>
<td>CRP</td>
<td>26.9 (23.1–31.0)</td>
<td>31.1 (27.2–35.4)</td>
<td>—</td>
<td>17.9 (14.6–21.6)</td>
<td>8.00</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>69.5 (65.2–73.4)</td>
<td>43.6 (41.1–50.1)</td>
<td>—</td>
<td>34.1 (30.1–36.5)</td>
<td>25.85</td>
</tr>
<tr>
<td>CXR</td>
<td>51.2 (46.7–55.7)</td>
<td>76.3 (72.2–79.9)</td>
<td>74.5 (70.3–78.2)</td>
<td>21.1 (17.7–25.2)</td>
<td>32.05</td>
</tr>
<tr>
<td>PPD</td>
<td>26.9 (23.1–31.0)</td>
<td>64.7 (60.2–68.8)</td>
<td>—</td>
<td>18.5 (15.2–22.2)</td>
<td>20.00</td>
</tr>
<tr>
<td>VDRL + FTA-ABS</td>
<td>56.2 (51.7–60.6)</td>
<td>73.5 (69.3–77.2)</td>
<td>—</td>
<td>18.1 (14.8–21.8)</td>
<td>10.34</td>
</tr>
<tr>
<td>ANA</td>
<td>43.8 (39.4–48.2)</td>
<td>39.2 (34.8–43.6)</td>
<td>9.6 (7.2–12.6)</td>
<td>43.2 (41.0–49.7)</td>
<td>18.10</td>
</tr>
<tr>
<td>ACE</td>
<td>34.5 (30.4–38.9)</td>
<td>60.0 (55.6–64.3)</td>
<td>63.5 (59.0–67.6)</td>
<td>16.7 (13.5–20.2)</td>
<td>19.65</td>
</tr>
<tr>
<td>ANCA</td>
<td>9.8 (7.4–12.8)</td>
<td>21.5 (18.0–25.4)</td>
<td>4.8 (3.2–7.1)</td>
<td>6.6 (4.6–9.3)</td>
<td>55.00</td>
</tr>
<tr>
<td>SI x-ray</td>
<td>41.0 (36.6–45.4)</td>
<td>22.9 (19.3–26.8)</td>
<td>—</td>
<td>4.6 (3.0–6.9)</td>
<td>31.50</td>
</tr>
<tr>
<td>S-Ca</td>
<td>7.2 (5.2–9.9)</td>
<td>21.1 (17.9–25.3)</td>
<td>28.7 (24.8–32.9)</td>
<td>4.8 (3.2–7.1)</td>
<td>2.59</td>
</tr>
<tr>
<td>Lyme</td>
<td>8.8 (6.5–11.7)</td>
<td>18.9 (15.6–22.6)</td>
<td>—</td>
<td>9.0 (6.7–11.9)</td>
<td>31.02</td>
</tr>
<tr>
<td>RF</td>
<td>36.9 (32.7–41.3)</td>
<td>31.3 (27.4–35.6)</td>
<td>—</td>
<td>44.8 (40.3–49.2)</td>
<td>3.10</td>
</tr>
<tr>
<td>CT chest</td>
<td>—</td>
<td>—</td>
<td>12.4 (9.7–15.7)</td>
<td>—</td>
<td>78.15</td>
</tr>
<tr>
<td>PFT</td>
<td>—</td>
<td>—</td>
<td>6.0 (4.2–8.5)</td>
<td>—</td>
<td>69.78</td>
</tr>
<tr>
<td>Gallium</td>
<td>—</td>
<td>—</td>
<td>9.0 (6.7–11.9)</td>
<td>—</td>
<td>237.95</td>
</tr>
</tbody>
</table>

*Forouohan et al.*

Note: CBC, complete blood count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; HLA-B27, human leukocyte antigen B27; CXR, chest x-ray; PPD, purified protein derivative tuberculin skin test; VDRL + FTA-ABS, Venereal Disease Research Laboratory and fluorescent treponemal antibody absorption; ANA, antinuclear antibody; ACE, angiotensin-converting enzyme; ANCA, antineutrophil cytoplasmic antibody; SI x-ray, sarcoidal x-ray; S-Ca, serum calcium level; Lyme, Lyme serology; RF, rheumatoid factor; CT chest, computed tomogram of the chest; PFT, pulmonary function test; Gallium, full-body gallium scan.
Monte Carlo simulation

A Monte Carlo simulation places a hypothetical cohort of patients through a mathematical model, and an outcome is observed. This is in contrast to obtaining an expected outcome such as with a decision tree model. Analogous to a clinical study, when a Monte Carlo simulation is repeated, the results will differ slightly each time. However, if a very large cohort of patients were put through the Monte Carlo simulation, the observed outcome would approximate the expected value from a classic decision analysis output. In addition, a Monte Carlo simulation provides a measure of variability. In this study, we performed a Monte Carlo simulation with 15,000 hypothetical patients undergoing diagnostic workup for anterior uveitis under the 4 different clinical scenarios. This sample size was chosen to simulate the number of new persons diagnosed with anterior uveitis annually in Canada. Results of the Monte Carlo simulation were reported, including mean, median, standard deviation, and range. In this way, a measure of variability for the model was obtained.

Cost savings in Canada

Using the results from our econometric model, we estimated the potential cost savings in Canada if the CNUS guidelines were implemented. An estimate of the annual incidence of anterior uveitis was calculated based on weighted averages obtained from the uveitis literature. The Canadian population was estimated at 31.6 million. The average cost savings per new patient with anterior uveitis were based on our cost-minimization analysis using the nongranulomatous uveitis in an adult model, under the assumption that the vast majority of new diagnoses of anterior uveitis would fall into this category.

RESULTS

Data from the CNUS included responses from 498 Canadian ophthalmologists, fellows, and residents, representing 42% of those surveyed. The actual practice pattern for the investigation of different anterior uveitis scenarios, based on results from the CNUS survey, is shown in Table 2. Based on the data from the CNUS, ophthalmologists consistently ordered more tests than were recommended by proposed guidelines, across all of the clinical scenarios studied (p < 0.05, 1-sample t test). Overall, complete blood count, erythrocyte sedimentation rate, C-reactive protein, antinuclear antibody, and rheumatoid factor were the most commonly ordered extraneous tests that were not included in the evidence-based guidelines for the routine investigation of anterior uveitis.

The results of our economic models are shown in Table 3. In every clinical scenario analyzed, the recommended guidelines imparted cost savings. The maximum additional cost was associated with nongranulomatous anterior uveitis in an adult, where more than $75 additional cost per patient was incurred. In contrast, only an additional $11 per patient was spent for a child with nongranulomatous anterior uveitis. Thus, following the recommended guidelines as shown in Table 1 is considered the dominant economic strategy in all clinical scenarios.

Sensitivity analyses show that our results are extremely robust. When the probability of ordering diagnostic tests based on current practice in Canada was varied to the lowest end of the 95% confidence interval for all diagnostic tests simultaneously, recommended guidelines were the dominant strategy for all clinical scenarios (Table 4). In addition, when costs were varied within ±10% of baseline, recommended guidelines continued to be the dominant strategy (Table 4). In fact, when both probabilities and costs were varied simultaneously, the recommended guidelines were still dominant, indicating an extremely robust model (Table 5).

Table 6 shows the results of the Monte Carlo simulation across all 4 clinical scenarios. This model showed that there was an observed cost savings from implementing the CNUS guidelines compared with current practice patterns when 15,000 patients were hypothetically analyzed. These cost savings were similar to the results obtained from our econometric model (Table 3). In addition, we obtained measures of variability in our estimate for cost savings (i.e., standard deviation and range) in each scenario (Table 6).

Based on the uveitis epidemiology literature, the annual incidence of anterior uveitis, based on a weighted
average of published incidence rates, was estimated at 0.024% per annum.\(^9\)–\(^18\) Applying this incidence rate to the Canadian population, following the guidelines shown in Table 1 would result in a net cost savings of approximately $600,000 per annum.

**INTERPRETATION**

Given the vast array of diagnostic possibilities available to investigate a patient presenting with anterior uveitis, it is not surprising that most ophthalmologists entertain some battery of investigations to guide their management. Indeed, given the appropriate circumstances, ancillary testing can be useful; positive test results can provide diagnostic clues, guide treatment, and rule out serious systemic associations.\(^2\) Determining the exact etiology of anterior uveitis is useful for both diagnostic and therapeutic reasons. This is particularly true in the advent of newer biologic agents that are more selective in treating specific components of the inflammatory cascade and may be more specific for certain types of inflammatory diseases. However, nonselective testing not only can be wasteful, but also can confound the management of such patients as, inevitably, each investigation suffers from limitations such as false-positive and false-negatives results.\(^20\) Clearly, selecting appropriate testing must be done within the context of the clinical situation in which a patient presents.\(^21\) As opposed to referring the patient to an internist for a broad-based investigative approach, ophthalmologists are uniquely able to specifically direct the workup of such patients, based on the diagnostic clues of a thorough ocular examination.

The CNUS described the current practice pattern of Canadian ophthalmologists in the routine investigation of anterior uveitis, and published evidence-based guidelines for such investigations. The findings in the present study suggest that a consistent, evidence-based approach is not the current standard of practice in Canada. Ophthalmologists were found to consistently order more tests than recommended by the literature, with the excess testing providing additional, unnecessary costs to the health care system. Furthermore, the findings of the present study suggest that following the published guidelines represents a cost-saving strategy. Indeed, the results of the cost-minimization analysis, confirmed by the sensitivity analyses, showed that extra costs in the range of $11 to $75 are incurred per patient investigated when compared with those projected by adherence to the recommended guidelines. When applied to the Canadian population, this may result in cost savings of $600,000 per year. The fact that these results were maintained in the basic and 2-way sensitivity analyses further underscores the validity of the difference in costs detected in the cost-minimization analysis. This suggests that the CNUS guidelines shown in Table 1 represent not only an evidence-based reference but also a clinically useful and cost-effective framework on which to guide the routine investigation of anterior uveitis in Canada.

Estimating annual cost savings depends on obtaining accurate data on the incidence of anterior uveitis in Canada. Although no direct Canada-specific data were found, we estimated incidence data based on multiple sources.\(^9\)–\(^18\) The annual incidence of uveitis has been estimated to be about 17 to 52 per 100,000 (i.e., 0.017% to 0.052%), with anterior uveitis accounting for nearly 50% to 60% of all cases.\(^10\) Recently, Gritz et al.\(^9\) published results estimating an incidence of uveitis of 0.05% in a population of Northern Californians, with a 0.037% incidence of anterior uveitis. These results are higher than those traditionally quoted. Our estimations, based on weighted averages of published incidence rates of anterior uveitis, suggested an annual incidence of approximately 0.024%. It is interesting that the study by Gritz et al. also suggested that the prevalence of uveitis may actually increase with age.\(^9\) If this is true, instituting the proposed guidelines is even more important in light of the aging Canadian population.

There are many possible explanations as to why Canadian ophthalmologists appear to order extraneous tests in the workup of anterior uveitis. Clinicians may entertain a broad approach in their investigation for fear of missing certain diagnoses, or they may simply feel that such an approach is what is required or recommended by the medical literature.\(^20\) Indeed, many of the extraneous tests that have been identified as providing no real diagnostic benefit are cited in textbooks and older literature as recommended investigations.\(^2\) Given that the CNUS guidelines are up to date, evidence based, and cost effective, it is hoped that they will become a commonly used tool to aid clinical decision making. It should be reiterated that the CNUS guidelines represent recommendations for the routine investigation of anterior uveitis and are intended to guide,

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**Table 5—Two-way sensitivity analysis**

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Sensitivity analysis ($)(^*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Nongranulomatous anterior uveitis, adult</td>
<td>58.33</td>
</tr>
<tr>
<td>Granulomatous anterior uveitis, adult</td>
<td>26.09</td>
</tr>
<tr>
<td>Anterior uveitis, suspected sarcoidosis, adult or child</td>
<td>20.25</td>
</tr>
<tr>
<td>Anterior uveitis, child</td>
<td>3.15</td>
</tr>
</tbody>
</table>

\(^*\)Costs varied (+10%) and probabilities of diagnostic tests being ordered varied over 95% confidence intervals simultaneously (cost savings).

**Table 6—Monte Carlo simulation (cost savings per patient using recommended guidelines; \(n = 15,000\)**

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Mean cost per patient ($)</th>
<th>Standard deviation ($)</th>
<th>Median ($)</th>
<th>Range ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nongranulomatous anterior uveitis, adult</td>
<td>74.20</td>
<td>34.00</td>
<td>73.00</td>
<td>0–210</td>
</tr>
<tr>
<td>Granulomatous anterior uveitis, adult</td>
<td>38.00</td>
<td>38.00</td>
<td>36.00</td>
<td>0–154</td>
</tr>
<tr>
<td>Anterior uveitis, suspected sarcoidosis, adult or child</td>
<td>39.00</td>
<td>77.00</td>
<td>23.00</td>
<td>0–409</td>
</tr>
<tr>
<td>Anterior uveitis, child</td>
<td>10.00</td>
<td>30.00</td>
<td>6.00</td>
<td>0–161</td>
</tr>
</tbody>
</table>

**Note:** Data expressed in Canadian dollars.
not replace, clinical judgment. The astute clinician should tailor his or her investigation based on a detailed history and physical examination. It is also important to underscore the fact that guidelines are developed based on the best available medical literature, and our analysis is only meaningful if the guidelines studied are considered the best current practice recommendations. As we continue to learn more about uveitis, these recommendations may change. For example, urine testing for β₂-microglobulin was not originally recommended by the CNUS in the testing of nongranulomatous anterior uveitis in a child, but a recent study by Mackensen et al. suggests that this may be warranted. Hence, evidence-based guidelines for uveitis testing are likely to evolve over time.

The results of the present study appear to be statistically robust; however, there are several limitations. As mentioned, incidence data are based on estimates from non-Canadian populations; true incidence data in Canada may differ slightly. Also, the data used in the analyses are based on the survey results of Canadian physicians, and actual practice patterns may differ from those reported in the survey. Further, all cost-effectiveness analyses are influenced by inherent variabilities in both the costs and the probabilities of the item studied; this, however, did not appear to be a major issue in the present study because the sensitivity analyses showed that our results were still robust as both costs and probabilities were varied. Moreover, the cost-minimization analysis assumes that the 2 investigation patterns studied (the existing investigation pattern and the CNUS guideline recommendations) were equivalent with respect to the effectiveness of diagnosing anterior uveitis. Although we would not expect the evidence-based CNUS guidelines to be inferior to current practice patterns, this may not necessarily be the case. It was not the purpose of this study to investigate the diagnostic accuracy of the various tests used in the diagnosis of anterior uveitis. Finally, as mentioned previously, there may be clinical circumstances in which additional testing not recommended by the CNUS guidelines is warranted based on individual clinical circumstances; these situations were not considered in our analyses.

In summary, current practice patterns suggest that Canadian ophthalmologists order unnecessary tests in the routine investigation of anterior uveitis. The results of the cost analysis support our previous recommendations for investigation of anterior uveitis. Implementing evidence-based clinical guidelines can improve both the efficiency and cost-effectiveness of anterior uveitis investigation in Canada.

REFERENCES


Key words: anterior uveitis, iritis, investigation, testing, cost-effectiveness