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# Minimization of ragweed allergy immunotherapy costs through use of the sublingual immunotherapy tablet in Canadian children with allergic rhinoconjunctivitis

Anne K. Ellis<sup>1</sup>, Douglas P. Mack<sup>2,3</sup>, Rémi Gagnon<sup>4</sup>, Eva Hammerby<sup>5\*</sup>  and Sheena Gosain<sup>6</sup>

## Abstract

**Background** Allergy immunotherapy (AIT), in the form of subcutaneous immunotherapy (SCIT) with alum-precipitated aqueous extracts, SCIT with a modified ragweed pollen allergen tyrosine adsorbate (MRPATA; Pollinex<sup>®</sup>-R), or a sublingual immunotherapy (SLIT)-tablet are options for the treatment of ragweed pollen allergic rhinoconjunctivitis (ARC) in Canadian children. A cost minimization analysis evaluated the economic implications of the use of the ragweed SLIT-tablet vs SCIT in Canadian children with ragweed ARC.

**Methods** A cost minimization analysis was conducted comparing the short ragweed SLIT-tablet, 12 Amb a 1-U, preseasonally with preseasonal ragweed SCIT, annual ragweed SCIT, or MRPATA. The analysis was conducted over a time horizon of 3 years from a public payer perspective in Ontario and Quebec. Resources and costs associated with medication and services of healthcare professionals were considered for each treatment. The resource and cost input values for the model were obtained from published literature and validated by Canadian clinical experts in active allergy practice. A discount rate of 1.5% was applied. Several scenario analyses were conducted to determine the impact of many of the key base case assumptions on the outcomes.

**Results** Over the total 3-year time horizon, the ragweed SLIT-tablet had a potential cost savings of \$900.14 in Ontario and \$1023.14 in Quebec when compared with preseasonal ragweed SCIT, of \$6613.22 in Ontario and \$8750.64 in Quebec when compared with annual ragweed SCIT, and \$79.62 in Ontario and \$429.49 in Quebec when compared with MRPATA. The ragweed SLIT-tablet had higher drug costs compared with the other AIT options, but lower costs for healthcare professional services. The lower costs for healthcare professional services with the ragweed SLIT-tablet were driven by the need for fewer office visits than SCIT. Scenario analysis indicated that costs were most impacted by including societal costs (e.g., costs associated with patient/caregiver travel and time lost). The potential cost savings of the ragweed SLIT-tablet versus SCIT and MRPATA was maintained in most scenarios.

**Conclusions** In this cost minimization analysis, the ragweed SLIT-tablet provided estimated cost savings from a public payer perspective for the treatment of ragweed ARC in Canadian children compared with SCIT or MRPATA.

\*Correspondence:

Eva Hammerby

Eva.Hammerby@alk.net

Full list of author information is available at the end of the article



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**Keywords** Cost, Ragweed, Subcutaneous immunotherapy, Sublingual immunotherapy, Tablet, Allergic rhinoconjunctivitis, Children

## Introduction

Allergic rhinoconjunctivitis (ARC) affects adults and children worldwide. In Canada, a nationwide survey of adults found that 20% of the surveyed population had been diagnosed with ARC [1]. The symptoms of ARC interfere with daily activities and sleep and are associated with poor concentration, fatigue, and reduced productivity [1, 2]. Children with ARC also have reduced school productivity and performance [2, 3]. This impairment in academic performance has been suggested to significantly affect long-term employment success and economic earnings [4].

Ragweed is one of the most common allergens associated with ARC in Canada and is most prevalent in Ontario and Quebec [5]. In a study across Canada, 28% of adults in Hamilton, Ontario, and 33% in Montreal, Quebec, were sensitized to ragweed [6]. Symptom-relieving medications such as antihistamines and intranasal corticosteroids can be used to treat the symptoms of ARC but have no impact on the disease itself. Alternatively, allergy immunotherapy (AIT) treatment modifies the pathogenic mechanisms that drive ARC, with a subsequent reduction in ARC symptoms and symptom-relieving medication use that can last years after stopping treatment [7–9]. In addition, AIT has been demonstrated to be a cost-effective treatment for ARC compared with symptom-relieving medication [10].

Allergy immunotherapy options for ragweed ARC in Canada include preseasonal subcutaneous immunotherapy (SCIT), using either alum-precipitated aqueous extracts or a modified ragweed pollen allergen tyrosine adsorbate (MRPATA; Pollinex<sup>®</sup>-R, Allergy Therapeutics [UK] Limited, Worthing, UK), and the short ragweed sublingual immunotherapy (SLIT)-tablet, 12 Amb a 1-U (Ragwitek<sup>®</sup>, ALK-Abelló A/S, Hørsholm, Denmark) preseasonally. MRPATA is a commercial SCIT preparation approved in Canada for the treatment of ragweed ARC in adults and children (ages 8 years and up) [11]. The ragweed SLIT-tablet was approved in Canada for adults in 2014 and for children (ages 5 years and up) in 2021 to reduce the signs and symptoms of moderate to severe seasonal short ragweed pollen ARC [12]. SCIT is an effective option for the treatment of ARC [13], but the need for multiple injections and frequent clinic visits increases the economic burden on healthcare resources and is inconvenient for patients and their caregivers. In contrast, if tolerated, SLIT-tablets can be taken at home after the first dose is administered under medical

supervision in the clinic. SLIT is also considered to be safer than SCIT [14, 15]. Studies and patient surveys indicate that patients have a strong preference for SLIT over SCIT because of the convenience of at home administration and the more favorable safety profile [16–19]. For the same reasons, these preferences also translate to caregivers of children receiving AIT [19]. A cost minimization analysis was conducted to evaluate the economic implications of the use of the ragweed SLIT-tablet vs SCIT in Canadian children with ragweed ARC.

## Methods

### Cost minimization analysis

A cost minimization analysis was conducted to determine the cost impact of the ragweed SLIT-tablet, 12 Amb a 1-U versus other AIT comparators (e.g., ragweed SCIT prepared from alum-precipitated aqueous extracts or MRPATA) in Ontario and Quebec. A cost minimization analysis was chosen as the type of economic analysis because there are no available head-to-head efficacy and safety data between the ragweed SLIT-tablet and the comparators. It was conservatively assumed that the ragweed SLIT-tablet and the AIT comparators were therapeutically equivalent, despite evidence that SLIT has a more favorable safety profile than SCIT [14, 15]. The use of symptom-relieving medications for ARC symptoms was not included in the analysis based on the assumption that their use would be the same among the evaluated AIT options.

The analysis was conducted over a time horizon of 3 years, which is the minimum recommended duration of AIT treatment for seasonal pollens [8, 20]. The benefits and costs after completing 3 years of treatment were assumed to be the same for the ragweed SLIT-tablet and the AIT comparators. A public payer perspective relevant to Ontario or Quebec was adopted to estimate costs; therefore, no patient resources or costs (i.e., travel time/costs) were included in the base case model. A discount rate of 1.5% was applied in the base case model in accordance with Canadian economic evaluation guidelines [21].

The input values for the model were obtained from published literature and validated by Canadian clinical experts in active allergy practice.

### Model resource inputs

Medication resources and services of healthcare professionals were considered for each treatment

included in the analysis. These resources for the ragweed SLIT-tablet, ragweed SCIT, and MRPATA over a 3-year treatment period are summarized in Table 1.

Medication resource use was assumed to be the same for Ontario and Quebec. Using information from the Health Canada product monograph [12] for the base case analysis it was assumed that the ragweed SLIT-tablet would be taken once daily during the pre-season (starting at least 12 weeks before the pollen season) and continued through the pollen season, for a duration of 6 months [22]. This regimen was assumed to be repeated for years 2 and 3. There were 2 SCIT regimens compared in the analysis. The first SCIT regimen was pre-ragweed pollen season (preseasonal) monotherapy. The duration of preseasonal SCIT varies in practice from 8 to 13 weeks; a conservative estimate of 11 weekly preseasonal injections given during the titration phase, with 1 week between injections, and no yearly maintenance injections was assumed for the base case analysis. These assumptions were validated by Canadian clinical experts as representative of preseasonal SCIT treatment. The preseasonal SCIT regimen was assumed to be repeated for years 2 and 3. The second SCIT regimen was annual treatment, in which a base case of 25 weekly titration injections were assumed with 1 week between injections, followed by maintenance injections every 4 weeks. It was assumed that one 10 mL vial would last for 10 injections [23]. MRPATA was assumed in the base case to be administered by a healthcare provider in 4 weekly preseasonal injections. This regimen was assumed to be repeated for years 2 and 3.

The services of physicians and nurses are required in the assessment, prescribing, and administration of the ragweed SLIT-tablet, ragweed SCIT, and MRPATA. A key difference in healthcare resource use among the AIT options is that after the first dose is administered in the clinic, the ragweed SLIT-tablet is administered at-home. Therefore, for Ontario it was assumed that there would be one initial visit each year with a physician (95% specialist, 5% general practitioner) for the ragweed SLIT-tablet, as well as 30 min of observation time with a nurse. For Quebec, no nurse observation time was included in the base case analysis of the ragweed SLIT-tablet because it is not covered by the Régie de l'assurance maladie du Québec. In both Ontario and Quebec, one physician (90% specialist, 10% general practitioner) follow-up visit at the end of the treatment season was assumed for the ragweed SLIT-tablet. For Ontario, each ragweed SCIT injection and MRPATA injection was assumed to be associated with a physician injection administration fee, a physician consultation, and 30 min of observation time with a nurse. For Quebec, no nurse observation time was included in the base case analysis of ragweed SCIT

or MRPATA because it is not covered by the Régie de l'assurance maladie du Québec. For the base case analysis for both Ontario and Quebec, it was assumed that 90% of patients visited a specialist and 10% visited a general practitioner for the ragweed SCIT titration visits, 5% visited a specialist and 95% visited a general practitioner for ragweed annual SCIT maintenance visits, and that 20% of patients visited a specialist and 80% visited a general practitioner for the MRPATA visits.

#### Model cost inputs

Costs associated with medication and services of healthcare professionals were considered for each treatment included in the analysis. All costs are in Canadian dollars. The costs for the ragweed SLIT-tablet, ragweed SCIT, and MRPATA over a 3-year treatment period for Ontario and Quebec are summarized in Table 2.

The medication costs were obtained from the manufacturer submitted price for the ragweed SLIT-tablet, from the Régie de l'assurance maladie du Québec [24] for ragweed SCIT, and the Association québécoise des pharmaciens propriétaires [25] for MRPATA. There are multiple inputs for ragweed SCIT costs as there are varied formulations for pre-seasonal and annual treatments. The mark-up for Ontario (8%) and Quebec (6.5%) was obtained from the Patented Medicine Prices Review Board [26]. The dispensing fee for Ontario (\$8.83/claim) was obtained from the Ontario Ministry of Health and Long-Term Care [27] and for Quebec (\$9.94/claim) was obtained from Patented Medicine Prices Review Board [26]. It was assumed that the costs did not change over the 3-year time horizon of the analysis.

Costs for physician services in Ontario were obtained from the Ontario Schedule of Benefits and Fees [28] and for Quebec were obtained from the RAMQ Manuel des Médecins Spécialistes [29]. Costs for nurse services in Ontario were obtained from the Ontario Nurses' Association collective agreement (assumes 8 years experience, \$48.17/hour plus 4.8% for vacation and 13% for fringe benefits, totaling \$56.74/hour) [30].

#### Scenario analyses

Several scenario analyses were conducted to determine the impact of many of the key base case assumptions on the outcomes. The different scenarios examined variable discount rates, more MRPATA injections, a lower proportion of specialist titration visits for ragweed SCIT, shorter ragweed SLIT-tablet treatment course, more or less nurse times per SCIT injection (for Ontario only since nursing costs are not covered in Quebec), exclusion of markup and dispensing fees, and addition of nursing costs for Quebec. Scenarios were also considered that



**Table 1** (continued)

| Resource                             | Ontario                |                          |                      |                        | Quebec                 |                          |  |                        |
|--------------------------------------|------------------------|--------------------------|----------------------|------------------------|------------------------|--------------------------|--|------------------------|
|                                      | Ragweed SLIT-tablet    | Preseasonal ragweed SCIT | Annual SCIT          | MRPATA                 | Ragweed SLIT-tablet    | Preseasonal ragweed SCIT | Annual SCIT                                  | MRPATA                 |
|                                      | Years 1, 2, and 3 each | Years 1, 2, and 3 each   | Year 1 Year 2 Year 3 | Years 1, 2, and 3 each | Years 1, 2, and 3 each | Years 1, 2, and 3 each   | Year 1 Year 2 Year 3                         | Years 1, 2, and 3 each |
| GP (20%)                             | 0                      | 0.2                      | 0.2 0.2 0.2          | 0.2 0.2                | 0                      | 0.2                      | 0.2 0.2 0.2                                  | 0.2                    |
| Specialist (80%)                     | 0                      | 0.8                      | 0.8 0.8 0.8          | 0.8 0.8                | 0                      | 0.8                      | 0.8 0.8 0.8                                  | 0.8                    |
| Nurse: time worked for injections, h | 0                      | 5.50                     | 15.88 6.50 6.50      | 2.00 2.00              | 0                      | 0 <sup>a</sup>           | 0 <sup>a</sup> 0 <sup>a</sup> 0 <sup>a</sup> | 0 <sup>a</sup>         |

GP general practitioner, MRPATA modified ragweed pollen allergen tyrosine adsorbate, SCIT subcutaneous immunotherapy, SLIT sublingual immunotherapy  
<sup>a</sup> No nurse observation time was included because it is not covered by the Régie de l'assurance maladie du Québec

**Table 2** Model cost inputs for medication and services of healthcare professionals in Ontario and Quebec

| Cost category        | Cost type   |   | \$/CAD/Unit |          |
|----------------------|---|---|-------------|----------|
|                      | Ontario   | Quebec  | Ontario     | Quebec   |
| Ragweed SLIT-tablets | Box of 30 tablets   |   | \$117.31    | \$117.31 |
|                      | Mark-up(27)   |   | 8%          | 6.5%     |
|                      | Dispensing fee/claim(27, 28)  |   | \$8.83      | \$9.94   |
| Ragweed SCIT vials   | Complete Treatment Set—Monovalent standardized [Omega (99100075)] per treatment(25) |   | \$265.00    | \$265.00 |
|                      | 10 mL maintenance—Monovalent standardized [Omega (02247754)] per vial(25)           |   | \$265.00    | \$265.00 |
|                      | Complete Treatment Set—Preseasonal Ragweed [Omega (99101150)] per treatment(25)     |   | \$265.00    | \$265.00 |
| MRPATA               | MRPATA [Paladin (00464988)] single vial(26)   |   | \$111.60    | \$111.60 |
|                      | MRPATA [Paladin (00464988)] per treatment (4 vials)                                 |   | \$446.72    | \$446.72 |
| Physician            | Medical specific re-assessment (follow-up visit)—A624(29)                           | Main visit—(09150 50% institution and 09127 50% private clinic)(30)   | \$62.05     | \$93.10  |
|                      | Partial assessment (pre- or post-injection) with specialist—A628(29)                | Control visit—(09152 50% institution and 09129 50% private clinic)(30)  | \$38.55     | \$53.38  |
|                      | Injection (sole reason for visit)—G212(29)  | Allergen immunotherapy including professional participation in the process, if necessary, and interpretation—one injection—20105 (50% institution and 50% private clinic)(30) | \$9.75      | \$26.28  |
|                      | Injection (with consultation at same visit)—G202(29)                                |   | \$4.45      | -        |
|                      |   |   |             |          |
| Nurse                | Hourly wage (2020)(31)  |   | \$56.74     | -        |

CAD Canadian dollars, MRPATA modified ragweed pollen allergen tyrosine adsorbate, SCIT subcutaneous immunotherapy, SLIT sublingual immunotherapy

assessed the economic impact of the ragweed SLIT-tablet from a societal or patient perspective rather than the payer perspective used in the base case analysis. The patient resources assumed for the societal or patient perspective scenario include patient time lost for office visits and travel distance, details of which are described in Additional file 1: Table S1. The assumed patient costs associated with time lost were an average hourly wage (as of December 2022 for individuals aged 16 years and older) of \$30.49 in Ontario and \$24.39 in Quebec obtained from Statistics Canada [31]. The assumed cost associated with travel distance by private car for the first 5000 km driven was \$0.59 in Ontario and \$0.47 per kilometer in Quebec obtained from the Canadian 2020 Reasonable Kilometer-Allowance rates [32].

A scenario that included nurse working time was conducted for Quebec, where it was excluded from the base case scenario because of lack of public plan coverage. For this scenario, the nurse work time in hours was 0 (years 1, 2, and 3 each) for ragweed SLIT-tablet, 5.50 (years 1, 2, and 3 each) for preseasonal SCIT, 15.88 (year 1), 6.50 (year 2), and 6.50 (year 3) for annual SCIT, and 2.0 (years 1, 2, and 3 each) for MRPATA.

## Results

### Costs of ragweed SLIT-tablet and AIT comparators

The total healthcare costs for 3 years of treatment for ragweed SLIT-tablet was \$2700.86 in Ontario and

\$2826.12 in Quebec, for preseasonal ragweed SCIT was \$3601.00 in Ontario and \$3849.25 in Quebec, for annual ragweed SCIT was \$9314.08 in Ontario and \$11,576.96 in Quebec, and for MRPATA was \$2780.48 in Ontario and \$3255.61 in Quebec (Table 3). Yearly costs were the same or similar within each AIT option. Total healthcare costs for all the evaluated AIT options were higher in Quebec than Ontario. Drug costs were the primary cost drivers for the ragweed SLIT-tablet and MRPATA, whereas healthcare professional services were the primary cost drivers for preseasonal and annual ragweed SCIT.

Over the total 3-year time horizon, the ragweed SLIT-tablet had a potential cost savings of \$900.14 in Ontario and \$1023.14 in Quebec when compared with preseasonal ragweed SCIT, of \$6613.22 in Ontario and \$8750.64 in Quebec when compared with annual ragweed SCIT, and \$79.62 in Ontario and \$429.49 in Quebec when compared with MRPATA (Table 4). The ragweed SLIT-tablet had higher drug costs compared with the other AIT options, but lower costs for healthcare professional services. The lower costs for healthcare professional services with the ragweed SLIT-tablet were driven by the need for fewer office visits than SCIT.

### Scenario analyses

Results from the scenario analysis indicated that costs were most impacted by including societal costs, which added patient costs and assumed 100% of patients

**Table 3** Yearly and total healthcare costs of ragweed SLIT-tablet, preseasonal ragweed SCIT, annual ragweed SCIT, and MRPATA in Ontario and Quebec (\$CAD)

| Cost category                 | Ontario          |                  |                  |                              | Quebec           |                  |                  |                              |
|-------------------------------|------------------|------------------|------------------|------------------------------|------------------|------------------|------------------|------------------------------|
|                               | Year 1           | Year 2           | Year 3           | Total Years 1–3 (discounted) | Year 1           | Year 2           | Year 3           | Total Years 1–3 (discounted) |
| Ragweed SLIT-tablet           |                  |                  |                  |                              |                  |                  |                  |                              |
| Drug costs                    | \$813.12         | \$813.12         | \$813.12         | \$2403.50                    | \$809.23         | \$809.23         | \$809.23         | \$2391.98                    |
| Tablet costs                  | \$703.84         | \$703.84         | \$703.84         | \$2080.46                    | \$703.84         | \$703.84         | \$703.84         | \$2080.46                    |
| Markup and dispensing fees    | \$109.29         | \$109.29         | \$109.29         | \$323.04                     | \$105.39         | \$105.39         | \$105.39         | \$311.52                     |
| Physician costs               | \$100.60         | \$100.60         | \$100.60         | \$297.36                     | \$199.85         | \$119.79         | \$119.79         | \$434.14                     |
| GP                            | \$59.70          | \$59.70          | \$59.70          | \$176.47                     | \$14.65          | \$10.64          | \$10.64          | \$35.47                      |
| Specialist                    | \$40.90          | \$40.90          | \$40.90          | \$120.90                     | \$185.20         | \$109.14         | \$109.14         | \$398.67                     |
| <b>Total healthcare costs</b> | <b>\$913.72</b>  | <b>\$913.72</b>  | <b>\$913.72</b>  | <b>\$2700.86</b>             | <b>\$1009.08</b> | <b>\$929.01</b>  | <b>\$929.01</b>  | <b>\$2826.12</b>             |
| Preseasonal ragweed SCIT      |                  |                  |                  |                              |                  |                  |                  |                              |
| Drug costs                    | \$295.03         | \$295.03         | \$295.03         | \$872.07                     | \$292.17         | \$292.17         | \$292.17         | \$863.61                     |
| Vial costs                    | \$265.00         | \$265.00         | \$265.00         | \$783.31                     | \$265.00         | \$265.00         | \$265.00         | \$783.31                     |
| Markup and dispensing fees    | \$30.03          | \$30.03          | \$30.03          | \$88.77                      | \$27.17          | \$27.17          | \$27.17          | \$80.30                      |
| Physician costs               | \$611.13         | \$611.13         | \$611.13         | \$1806.41                    | \$1010.07        | \$1010.07        | \$1010.07        | \$2985.65                    |
| Injection                     | \$117.98         | \$117.98         | \$117.98         | \$348.72                     | \$317.93         | \$317.93         | \$317.93         | \$939.76                     |
| GP                            | \$107.25         | \$107.25         | \$107.25         | \$317.02                     | \$289.03         | \$289.03         | \$289.03         | \$854.32                     |
| Specialist                    | \$10.73          | \$10.73          | \$10.73          | \$31.70                      | \$28.90          | \$28.90          | \$28.90          | \$85.43                      |
| Consultation costs            | \$493.15         | \$493.15         | \$493.15         | \$1457.69                    | \$692.14         | \$692.14         | \$692.14         | \$2045.89                    |
| GP                            | \$80.67          | \$80.67          | \$80.67          | \$238.44                     | \$121.03         | \$121.03         | \$121.03         | \$357.75                     |
| Specialist                    | \$412.49         | \$412.49         | \$412.49         | \$1219.26                    | \$571.11         | \$571.11         | \$571.11         | \$1688.14                    |
| Nurse costs                   | \$312.09         | \$312.09         | \$312.09         | \$922.51                     | \$0.00           | \$0.00           | \$0.00           | \$0.00                       |
| <b>Total healthcare costs</b> | <b>\$1218.25</b> | <b>\$1218.25</b> | <b>\$1218.25</b> | <b>\$3601.00</b>             | <b>\$1302.24</b> | <b>\$1302.24</b> | <b>\$1302.24</b> | <b>\$3849.25</b>             |
| Annual ragweed SCIT           |                  |                  |                  |                              |                  |                  |                  |                              |
| Drug cost                     | \$590.06         | \$590.06         | \$590.06         | \$1,744.15                   | \$584.33         | \$584.33         | \$584.33         | \$1727.21                    |
| Vial costs                    | \$530.00         | \$530.00         | \$530.00         | \$1,566.62                   | \$530.00         | \$530.00         | \$530.00         | \$1566.62                    |
| Markup and dispensing fees    | \$60.06          | \$60.06          | \$60.06          | \$177.53                     | \$54.33          | \$54.33          | \$54.33          | \$160.59                     |
| Physician costs               | \$2284.02        | \$1873.16        | \$1873.16        | \$5947.71                    | \$3793.45        | \$3096.35        | \$3096.35        | \$9849.55                    |
| Injection                     | \$396.46         | \$247.16         | \$247.16         | \$879.88                     | \$1068.41        | \$666.07         | \$666.07         | \$2371.16                    |
| GP                            | \$309.56         | \$126.75         | \$126.75         | \$557.47                     | \$834.23         | \$341.58         | \$341.58         | \$1502.31                    |
| Specialist                    | \$86.90          | \$120.41         | \$120.41         | \$322.41                     | \$234.18         | \$324.50         | \$324.50         | \$868.85                     |
| Consultation costs            | \$1887.56        | \$1626.00        | \$1626.00        | \$5067.83                    | \$2725.04        | \$2430.28        | \$2430.28        | \$7478.38                    |
| GP                            | \$963.33         | \$1545.05        | \$1545.05        | \$3985.25                    | \$1445.38        | \$2318.19        | \$2318.19        | \$5979.49                    |
| Specialist                    | \$924.24         | \$80.96          | \$80.96          | \$1082.57                    | \$1279.67        | \$112.09         | \$112.09         | \$1498.90                    |
| Nurse costs                   | \$900.82         | \$368.84         | \$368.84         | \$1622.22                    | \$0.00           | \$0.00           | \$0.00           | \$0.00                       |
| <b>Total healthcare costs</b> | <b>\$3774.90</b> | <b>\$2832.06</b> | <b>\$2832.06</b> | <b>\$9314.08</b>             | <b>\$4377.78</b> | <b>\$3680.68</b> | <b>\$3680.68</b> | <b>\$11,576.76</b>           |
| MRPATA                        |                  |                  |                  |                              |                  |                  |                  |                              |
| Drug cost                     | \$491.29         | \$491.29         | \$491.29         | \$1452.19                    | \$485.70         | \$485.70         | \$485.70         | \$1435.66                    |
| Vial costs                    | \$446.72         | \$446.72         | \$446.72         | \$1320.45                    | \$446.72         | \$446.72         | \$446.72         | \$1320.45                    |
| Markup and dispensing fees    | \$44.57          | \$44.57          | \$44.57          | \$131.74                     | \$38.98          | \$38.98          | \$38.98          | \$115.21                     |
| Physician costs               | \$380.45         | \$380.45         | \$380.45         | \$1124.57                    | \$654.68         | \$654.68         | \$654.68         | \$1935.16                    |
| Injection                     | \$70.20          | \$70.20          | \$70.20          | \$207.50                     | \$189.18         | \$189.18         | \$189.18         | \$559.19                     |
| GP                            | \$39.00          | \$39.00          | \$39.00          | \$115.28                     | \$105.10         | \$105.10         | \$105.10         | \$310.66                     |
| Specialist                    | \$31.20          | \$31.20          | \$31.20          | \$92.22                      | \$84.08          | \$84.08          | \$84.08          | \$248.53                     |
| Consultation costs            | \$310.25         | \$310.25         | \$310.25         | \$917.06                     | \$465.50         | \$465.50         | \$465.50         | \$1375.96                    |
| GP                            | \$62.05          | \$62.05          | \$62.05          | \$183.41                     | \$93.10          | \$93.10          | \$93.10          | \$275.19                     |
| Specialist                    | \$248.20         | \$248.20         | \$248.20         | \$733.65                     | \$372.40         | \$372.40         | \$372.40         | \$1100.77                    |
| Nurse costs                   | \$113.49         | \$113.49         | \$113.49         | \$335.46                     | \$0.00           | \$0.00           | \$0.00           | \$0.00                       |
| <b>Total healthcare costs</b> | <b>\$940.66</b>  | <b>\$940.66</b>  | <b>\$940.66</b>  | <b>\$2780.48</b>             | <b>\$1101.40</b> | <b>\$1101.40</b> | <b>\$1101.40</b> | <b>\$3255.61</b>             |

CAD Canadian dollars, GP general practitioner, MRPATA modified ragweed pollen allergen tyrosine adsorbate, SCIT subcutaneous immunotherapy, SLIT sublingual immunotherapy

**Table 4** Potential healthcare cost savings with the ragweed SLIT-tablet vs preseasonal ragweed SCIT, annual ragweed SCIT, or MRPATA after 3 years of treatment (\$CAD)

| Cost category                 | Ontario   |  |                               | Quebec  |  |                               |
|-------------------------------|---|--|-------------------------------|---|--|-------------------------------|
|                               | Ragweed SLIT-tablet vs Preseasonal ragweed SCIT | Ragweed SLIT-tablet vs Annual ragweed SCIT | Ragweed SLIT-tablet vs MRPATA | Ragweed SLIT-tablet vs Preseasonal ragweed SCIT | Ragweed SLIT-tablet vs Annual ragweed SCIT | Ragweed SLIT-tablet vs MRPATA |
| Drug costs                    | \$1531.42                                       | \$659.35                                   | \$1083.04                     | \$1528.37                                       | \$664.76                                   | \$1071.52                     |
| Physician costs               | – \$1509.05                                     | – \$5,650.35                               | – \$827.20                    | – \$2551.51                                     | – \$9415.41                                | – \$1501.02                   |
| Nurse costs                   | – \$922.51                                      | – \$1,622.22                               | – \$335.46                    | \$0.00  | \$0.00                                     | \$0.00                        |
| <b>Total healthcare costs</b> | <b>– \$900.14</b>                               | <b>– \$6613.22</b>                         | <b>– \$79.62</b>              | <b>– \$1023.14</b>                              | <b>– \$8750.64</b>                         | <b>– \$429.49</b>             |

MRPATA modified ragweed pollen allergen tyrosine adsorbate, SCIT subcutaneous immunotherapy, SLIT sublingual immunotherapy

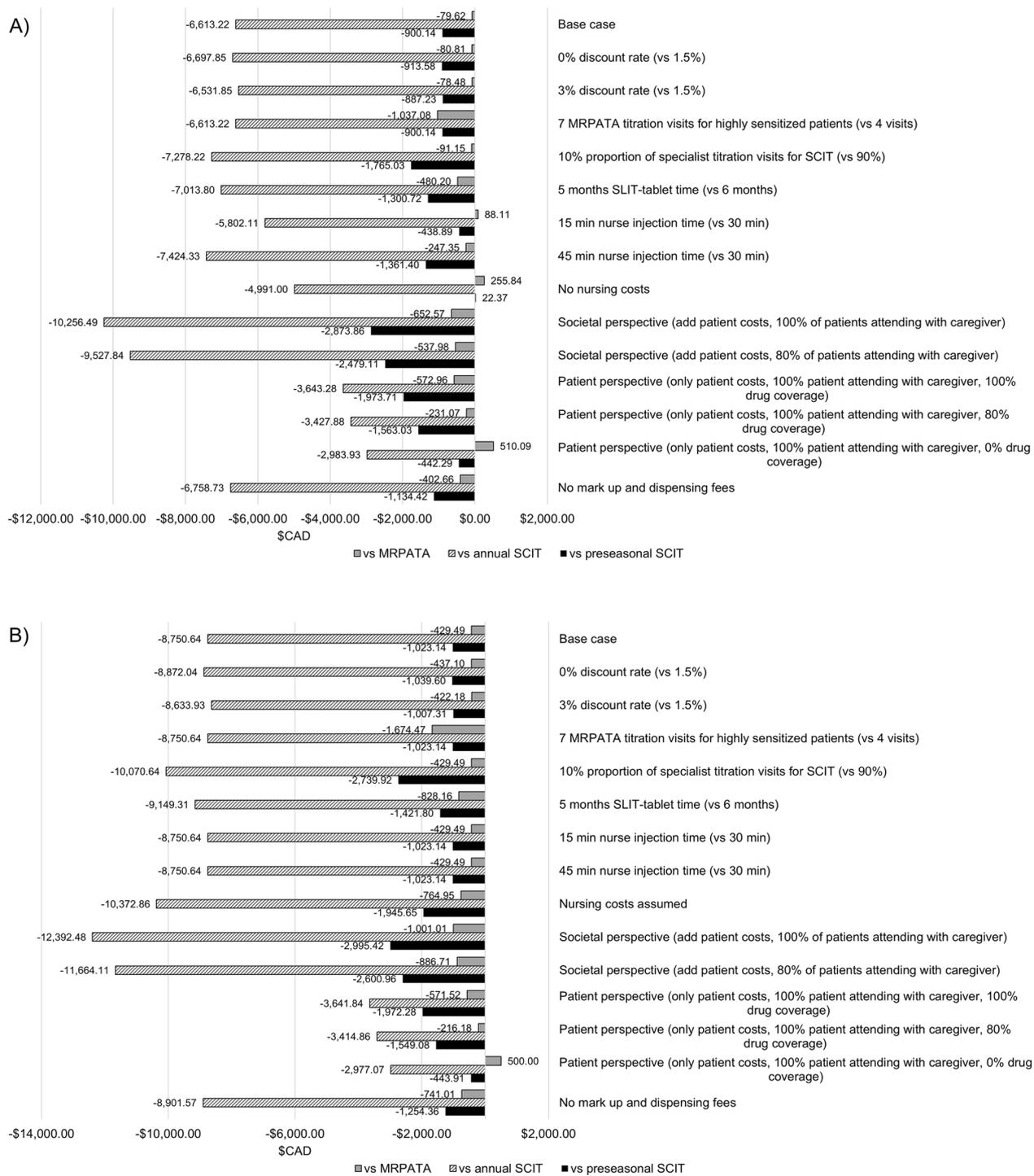
attended visits with a caregiver (Fig. 1A, B). Over the total 3-year time horizon, the ragweed SLIT-tablet from a societal perspective versus the base case had a substantial increase in the potential cost savings. Potential cost savings with the ragweed SLIT-tablet were \$2873.86 in Ontario and \$2995.42 in Quebec when compared with preseasonal ragweed SCIT, \$10,256.49 in Ontario and \$12,392.48 in Quebec when compared with annual ragweed SCIT, and \$652.57 in Ontario and \$1001.01 in Quebec when compared with MRPATA (Fig. 1A, B). There were 3 scenarios for Ontario in which the ragweed SLIT-tablet became more costly than an AIT comparator (vs MRPATA when assuming less nurse time per SCIT injection; vs preseasonal SCIT and MRPATA when assuming no nursing costs; and vs MRPATA when assessing only patient costs and assuming 100% patients attending with a caregiver and 0% drug coverage; Fig. 1A). For Quebec, the only scenario in which the ragweed SLIT-tablet became more costly than an AIT comparator was versus MRPATA when assessing only patient costs and assuming 100% patients attending with a caregiver and 0% drug coverage (Fig. 1B).

## Discussion

The results from this cost minimization analysis indicate that the ragweed SLIT-tablet provides potential cost savings compared with SCIT and MRPATA from a public payer perspective through 3 years of treatment. The cost savings is primarily because fewer clinic appointments are needed with the ragweed SLIT-tablet since it can be self-administered at home. Accordingly, the greatest potential cost savings with the ragweed SLIT-tablet were observed when compared with annual SCIT, which has the greatest number of required clinic visits. MRPATA requires only 4 injection clinic visits per year, and therefore has the smallest difference in cost savings versus the ragweed SLIT-tablet. Greater potential

cost-savings with the ragweed SLIT-tablet were observed in Quebec than Ontario, primarily driven by differences in physician costs. Scenario analyses found that the potential cost savings with ragweed SLIT-tablet versus SCIT became even greater from the societal perspective that incorporated the indirect costs of caregiver travel to clinic visits.

Cost minimization analyses have also been conducted with the house dust mite (HDM) SLIT-tablet, 12 SQ-HDM and white birch SLIT-tablet, 12 SQ-Bet in Canada [33, 34]. The analysis for the HDM SLIT-tablet was conducted from a societal perspective in Ontario and Quebec over a 3 year time period, and the comparator was HDM SCIT [33]. Potential cost savings of the HDM SLIT-tablet over HDM SCIT were \$1833 in Ontario and \$769 in Quebec. Similarly, the analysis for the white birch SLIT-tablet was also conducted from a societal perspective in Ontario and Quebec over a 3 year time period, and the comparator was preseasonal tree SCIT [34]. Potential cost savings of the white birch SLIT-tablet over preseasonal tree SCIT were \$1112 in Ontario and \$1200 in Quebec. The perspective was the major difference between the current analysis for the ragweed SLIT-tablet and the analyses conducted for the HDM and white birch SLIT-tablets. The HDM and white birch SLIT-tablet base case analyses were from a societal perspective that included patient travel costs and the lost hourly wages associated with clinic visits. Since larger numbers of clinic visits are needed for SCIT than the SLIT-tablets, these indirect patient costs are a key contributor to the cost savings with the SLIT-tablets. Similar findings were observed in the societal perspective scenario in the current ragweed SLIT-tablet analysis, although in this case the indirect cost was for the caregiver since it was assumed that every pediatric patient would be accompanied by an adult caregiver. These indirect costs are not inconsequential for the



**Fig. 1** Scenario analyses of potential cost savings after 3 years of treatment with ragweed SLIT-tablet vs pre-seasonal ragweed SCIT, annual ragweed SCIT, or MRPATA in **A)** Ontario and **B)** Quebec. *MRPATA* modified ragweed pollen allergen tyrosine adsorbate, *SCIT* subcutaneous immunotherapy, *SLIT* sublingual immunotherapy

patient and their families. For example, annual SCIT in the current analysis was assumed to result in 59 h of time spent in just the first year for clinic visits, which

at the assumed hourly wage comes to approximately \$1800 in lost wages in Ontario and \$1400 in Quebec. For patients and their caregivers living in rural areas,

the travel time and costs may be an even greater burden. In addition, although there are no associated costs, children have to miss school or after-school activities once a week for the first 6 months during the SCIT titration period and then monthly for subsequent maintenance visits. While it was not possible to quantify the actual patient cost for pediatric patients specifically, some adolescents may have to miss part-time work. Additional opportunity costs that could not be quantified for the patient should also be considered and may be substantial. The at-home administration of the SLIT-tablets has the added advantage of allowing patients to continue their treatment if in-person clinic visits need to be disrupted, as was the case during the early part of the COVID-19 pandemic.

Assumptions for the AIT options had to be made for the analysis and were based on published literature and input from experienced clinical experts. When some of these assumptions were explored in scenario analyses, including the number of MRPATA injections, nurse injection time, or the proportion of SCIT titration visits conducted by specialists versus general practitioners, the impact on the results was minimal. One input that did have a marked impact on the results was nursing costs. In some Canadian provinces, nurse-associated costs in public clinics are a cost for the healthcare system, whereas in private clinics the costs are funded out of the clinic's earnings. Therefore, in Ontario where nursing costs are covered by the public plan, removing the nursing costs decreased the potential cost savings of the ragweed SLIT-tablet from the public payer perspective. When nursing costs were added into the model for Quebec, where nursing costs are not covered by the public payer plan, there was an increase in the potential cost savings with the ragweed SLIT-tablet.

Ragweed SLIT-tablet treatment in the model had higher drug costs than SCIT or MRPATA. It was assumed in the analysis that the drug costs for the children were covered 100% under their caregiver's insurance or by a public plan. The scenario analyses indicated that ragweed SLIT-tablet treatment was more costly than MRPATA from the patient perspective when drug coverage was assumed to be 0%, but in this scenario, ragweed SLIT-tablet remained a cost saving alternative to SCIT.

There are some limitations for this cost minimization analysis. First, the model assumptions for the AIT resource use were validated by the clinical experts practicing in Ontario and Quebec, but AIT practice may vary by geographic region. In addition, adherence to treatment was considered to be 100% for all clinic visits and treatments. Adherence to both SLIT and SCIT has been demonstrated to be a challenge, [35,

36] and decreased adherence to clinic visits or the daily use of the SLIT-tablets would impact costs. However, children tend to be more adherent and are less likely to discontinue treatment than adults, possibly because their caregivers have a vested interest in ensuring an optimal outcome [37]. Another limitation is that because of the lack of head-to-head trials, efficacy was assumed to be equal among the AIT options. One study comparing MRPATA and SCIT using aqueous extracts found no improvement of symptoms with MRPATA [38]. Poorer efficacy could result in greater office visits for acute symptoms and greater symptom-relieving pharmacotherapy use, which in turn would increase costs. Another limitation is that the analysis did not consider patients who need AIT for polysensitization to allergens other than ragweed. Use of more than one concurrent SLIT-tablet is not currently approved. Studies have demonstrated the safety of dual SLIT-tablet administration, [39, 40] but efficacy of this practice has yet to be evaluated, and multiallergen SCIT may be needed for such patients.

## Conclusions

In this cost minimization analysis, the ragweed SLIT-tablet provided estimated cost savings from a public payer perspective for the treatment of ragweed ARC in Canadian children compared with SCIT or MRPATA. The potential cost savings with the ragweed SLIT-tablet were observed for both Ontario and Quebec and were maintained in most of the scenario analyses.

## Abbreviations

|        |   |
|--------|---|
| AIT    | Allergy immunotherapy                               |
| ARC    | Allergic rhinoconjunctivitis                        |
| CAD    | Canadian dollars                                    |
| HDM    | House dust mite                                     |
| MRPATA | Modified ragweed pollen allergen tyrosine adsorbate |
| SCIT   | Subcutaneous immunotherapy                          |
| SLIT   | Sublingual immunotherapy                            |

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13223-023-00758-7>.

**Additional file 1: Table S1.** Model patient resource inputs in Ontario and Quebec.

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## Author contributions

S. Gosain performed the data analyses. All authors interpreted the data and critically reviewed the manuscript. All authors read and approved the final manuscript.

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### Availability of data and materials

All data supporting the conclusions of this article are included within the article.

### Declarations

#### Ethics approval and consent to participate

Not applicable.

#### Consent for publication

Not applicable.

### Competing interests

A.K. Ellis has participated in advisory boards for Abbvie, ALK-Abelló, AstraZeneca, Bausch Health, Circassia Ltd, GlaxoSmithKline, LEO Pharma, Johnson & Johnson, Merck, Miravo, Mylan, Novartis, Pediapharm and Pfizer, has been a speaker for ALK, Aralez, AstraZeneca, Bausch Health, Boehringer-Ingelheim, CACME, Meda, Medexus, Mylan, Merck, Novartis, Pfizer, The ACADEMY, and Takeda. Her institution has received research grants from AstraZeneca, Bayer, LLC, Circassia Ltd, Green Cross Pharmaceuticals, GlaxoSmithKline, Sun Pharma, Merck, Novartis, Pfizer, Regeneron and Sanofi. She has also served as an independent consultant to Allergy Therapeutics, Bayer, LLC, Ora Inc., and Regeneron in the past. D. Mack has provided consultation and speaker services for Pfizer, Aimmune, Kaleo, Merck, Covis and Pediapharm, and has been part of an advisory board for Pfizer and Bausch Health. He sits on the editorial board for the Journal of Food Allergy and has served as an investigator for ALK-Abelló. R. Gagnon has served as a speaker and/or advisor for ALK-Abelló, AstraZeneca, Bausch Health, CSL Behring, GlaxoSmithKline, Merck, Novartis, Pfizer, Sanofi, and Shire, and Valeo Pharma, and served as an investigator for AstraZeneca, Amgen, Biocryst, DBV, GlaxoSmithKline, Green Cross Pharmaceuticals, Merck, Novartis, Pharvaris, Regeneron, Shire, Stallergenes, and Sanofi Genzyme/Regeneron. S. Gosain is an employee of PDCI Market Access Inc., which provided contracted services to ALK- Abelló A/S. E. Hammerby is an employee of ALK- Abelló A/S.

### Author details

<sup>1</sup>Division of Allergy & Immunology, Department of Medicine, Queen's University, Kingston, ON, Canada. <sup>2</sup>Department of Medicine, McMaster University, Hamilton, ON, Canada. <sup>3</sup>Halton Pediatric Allergy, Burlington, ON, Canada. <sup>4</sup>Clinique Spécialisée en Allergie de La Capitale, Québec, QC, Canada. <sup>5</sup>ALK-Abelló A/S, Hørsholm, Denmark. <sup>6</sup>PDCI Market Access, Inc, Ottawa, ON, Canada.

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