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Comparative Health-Care Cost Advantage of Ipratropium over Tiotropium in COPD Patients

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ABSTRACT

Objective: To compare the total direct health-care costs of patients treated with tiotropium and ipratropium. **Methods:** We conducted a cohort study of health-care costs in British Columbia, Canada, by comparing new patients on tiotropium with new patients on ipratropium. Direct health-care costs for study patients were measured in the first 2 years after initiating inhaled anticholinergic treatment. Differences in direct health-care costs between tiotropium and ipratropium patients were estimated by using quantile regression. We analyzed cost differences in the 10th percentile, median, and 90th percentile of patients by cost. High-dimensional propensity score analysis was used as a method of adjustment for potential confounding factors. **Results:** The study population had 3,140 tiotropium patients and 26,182 ipratropium patients. Higher health system costs in patients who started on tiotropium instead of ipratropium were observed in patients in the median and 10th percentile. The magnitude of these increases was comparable to the price difference between the two drugs. Health system costs in the 90th percentile were not significantly different between tiotropium and ipratropium patients. **Conclusions:** The results of this study did not support the preferential use of tiotropium over ipratropium as a basis for savings in direct health-care costs.

Keywords: COPD, health care, respiratory disease, tiotropium, utilization.

Introduction

Chronic obstructive pulmonary disease (COPD) is a major and growing cause of mortality and morbidity worldwide [1–3]. In North America, it is estimated that 19% of the population is living with the disease [4]. In Canada, in 2003, total direct health-care costs of COPD were estimated to be Can $1997 per patient [5]. In the United States, total direct health-care costs were estimated at US $4120 per patient [6]. More than half of all direct health-care costs in North American patients were inpatient hospital costs [5,6]. It has been argued that the burden of COPD could be curtailed by more extensive use of smoking cessation and pulmonary rehabilitation interventions and greater use of inhaled medications [5].

Inhaled anticholinergics (IACs) are among the most common medications used to treat COPD. The two IACs used most often are ipratropium bromide (Atrovent®) and tiotropium bromide (Spiriva®). Ipratropium is available as an aerosol inhaler and as a solution used with a nebulizer. Tiotropium is indicated for long-term maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema. It is a longer acting anticholinergic than ipratropium. Tiotropium is usually taken once a day in the form of capsules that are inserted into a handheld device and released as a powder when inhaled. In this regard, once-a-day tiotropium provides a convenience advantage over ipratropium, which, because it has a shorter duration of action, is usually taken in multiple inhalations throughout the day.

Tiotropium is considerably more expensive than ipratropium (CAN $2.49 per day prescription in 2009 compared with Can $1.30 for ipratropium). The cost difference and therapeutic substitutability of the drugs suggest that economic comparisons of the two could be useful to health-care insurers. If tiotropium results in better health outcomes than does ipratropium in otherwise similar patients, either because it is therapeutically superior or because convenience improves persistence on treatment, then better outcomes should translate to lower direct health-care expenditures in those patients so long as any reduction in medical costs exceed the additional cost of the drug.

In terms of existing evidence, meta-analyses of randomized trials have mixed results. Some suggested that tiotropium reduces COPD-related hospitalizations or exacerbation-related hospitalizations compared with placebo [7–9]. One of these meta-analyses also found a nonsignificant reduction in COPD-related hospitalizations with tiotropium in comparison with salmeterol [7]. One placebo-controlled trial measured all-cause hospitalizations and reported that tiotropium reduced all-cause hospitalizations [10].

Not all studies were unanimous. One trial that examined all-cause hospitalization did not find a significant difference [11], although it did report a significant improvement in hospitalizations

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due to COPD exacerbation in tiotropium patients. And one of two cohort studies evaluating COPD hospitalizations found a decreased risk of COPD referrals and hospitalizations with tiotropium as compared with ipratropium and salbutamol [12], while another found an increased risk of hospitalizations associated with tiotropium use as compared with nonuse [13]. In a time series analysis in British Columbia, there was a modest but statistically significant increase in emergency hospital admissions for COPD that coincided with the introduction of public drug coverage for tiotropium [14].

We conducted a population-based cohort study of direct health-care cost in British Columbia, Canada, in patients with COPD who were newly initiated on tiotropium or ipratropium. We compared the direct health-care system costs in both groups over the first 2 years of treatment and adjusted for potential confounding factors. The lack of consistency of results across available studies suggested that cost increases or decreases attributable to tiotropium were both plausible hypotheses. Therefore, we expected a priori that direct health-care costs in tiotropium patients could be either reduced or increased relative to ipratropium patients.

Methods

We designed a prospective cohort study by using data collected by the British Columbia Ministry of Health (MoH) between January 1, 2002, and December 31, 2008. The primary analysis assessed the total direct health-care costs from the perspective of the MoH. Secondary analyses examined hospital, physician services, and prescription drug costs separately. In British Columbia, all hospital costs and medically necessary physician visits were fully covered by the government. In addition, the government subsidized approximately half of all prescription drug costs.

All prescriptions that were dispensed at community pharmacies were recorded in a centralized database known as PharmaNet and were linkable using unique patient identifiers with a centralized Discharge Abstract Database for hospitalizations and a centralized Medical Services Plan database for physician visits. These databases included diagnostic codes (*International Classification of Diseases, Ninth Revision*, for physician visits and *International Statistical Classification of Diseases, Tenth Version,* for hospitalizations), procedure codes, service dates, admission dates, and death dates. We assumed that the completeness and misclassification of diagnostic coding was comparable to other administrative databases. Complete data were unavailable for federally insured patients such as Aboriginals, Royal Canadian Mounted Police, armed forces personnel, and prisoners. These groups comprised about 4% of the population.

Study population

The source population for the analysis included the person-time of all British Columbia residents who were at least 50 years of age between January 1, 2003, and December 31, 2006, and who were not federally insured for their medical coverage. The study population was drawn from the source population by extracting all prescriptions for tiotropium and ipratropium in the PharmaNet database that were dispensed between January 1, 2002, and December 31, 2006. These date ranges were chosen to maximize cohort enrolment while ensuring that study participants had at least 365 days of historical data preceding their first IAC prescription, and, similarly, up to 720 days of health-care utilization data available after initiating treatment. The study population included new users of ipratropium or tiotropium where new use was defined as no previous dispensing for an IAC in the previous year. We defined a study index date for each patient equal to the date of his or her first IAC dispensing. Patients were excluded from the analysis if they were younger than 50 years of age on their index date, were not enrolled in the Medical Service Plan for at least 1 year beforehand, if information on age or sex was missing, or if they were in a palliative care unit or long-term care facility prior to the index date.

Outcomes

Direct health-care costs were measured for each patient for up to 720 days after initiation on tiotropium or ipratropium. Patients were censored earlier than 720 days at the earliest occurrence of one of the following: switching between ipratropium and tiotropium, de-enrolment from the Medical Services Plan, or death. The primary outcome was total direct health-care costs, which we defined as the total sum of physician fee-for-service visit costs, hospitalization costs, and prescription drug costs. Each of the three component costs of total cost were analyzed separately as secondary outcomes. Each physician visit recorded in the Medical Services Plan database included the fee amount paid to the physician. For prescriptions, we used the ingredient cost amount and dispensing fee amounts charged by the pharmacy (regardless of payer). The actual cost of hospital stays is not calculated in Canada. Instead, hospitals receive global funding from their provincial MoH, and discharge records include a resource intensity weight (RIW) that can be used to estimate cost. RIWs are calculated by the Canadian Institute for Health Information. The RIW is an estimate of the relative amount of resources used by a patient during a hospital stay. Detailed information on RIW methodology can be obtained from www.cihi.ca. The British Columbia MoH estimates a dollar for an RIW by considering a number of factors including the total number of RIWs that a hospital accumulated and the amount of funding it received. As of June 22, 2009, the MoH in British Columbia estimated the cost of 1 RIW in the fiscal year 2008-2009 to be CAN $5012. For years prior to 2008/09, we used an adjusted RIW that when multiplied by CAN $5012 yielded the cost for the admission in 2008 dollars.

Statistical analysis

We conducted a modified high-dimensional propensity score (hdPS) analysis [15]. In the first step of the analysis, we identified five data dimensions: *International Classification of Diseases, Ninth Revision*, diagnoses in hospital records (first three digits), medical procedures in hospital records, *International Classification of Diseases, Ninth Revision,* diagnoses in physician visit records (first three digits), fee billing items in physician visit records, and American Hospital Formulary Service medication code in prescription drug records (fourth tier = eight digits). Next, we identified potential covariates in our study population by sorting codes within each of the five data dimensions according to their prevalence. Prevalence was measured as the proportion of patients having a specific code at least once during a 1-year baseline period. Because the prevalence of a binary factor is symmetrical around 0.5, we subtracted all prevalence estimates larger than 0.5 from 1.0. Codes were excluded from further analysis if less than 0.5% of patients or more than 99.5% of patients were identified as having it. We then selected up to 200 of the remaining codes from each data dimension for further analysis as potential covariates. From the up to 200 codes chosen from each data dimension we measured how frequently each code was recorded for each patient during the baseline period. We then divided each code into four binary variables for whether the code occurred: 1 time, the median number of times, the 75th percentile number of times, or the 90th percentile number of times. The 90th percentile was a modification to the original hdPS algorithm. A code that appeared above the 90th percentile number of times had a “true” value for all four recurrence variables. If any of the values were equal, the variable representing the lower cut point was excluded.

In each data dimension we estimated the amount of potential confounding that each covariate could produce in a multiplicative model according to the following formula:

$$\text{Bias}_{\text{Mult}} = \begin{cases} \dfrac{P_{C1}(RR_{CD}-1)+1}{P_{C0}(RR_{CD}-1)+1} & \text{if } RR_{CD} \geq 1 \\ \dfrac{P_{C1}[1/(RR_{CD})-1]+1}{P_{C0}[1/(RR_{CD})-1]+1} & \text{otherwise} \end{cases}$$

where P_{C1} and P_{C0} were the prevalence of the covariate (C) in the tiotropium (1) and ipratropium (0) patients, respectively, and RR_{CD} was the association between the potential confounder and a binary outcome indicator for cost (D). Conversion of the continuous cost variable to a binary indicator was done as a further modification to the hdPS algorithm and was done because the multiplicative bias formula was applicable to a binary outcome and a binary covariate. In performing this conversion, patients with health-care costs below the median cost were assigned a cost indicator value of 0. Patients at or above the median were assigned a value of 1. In a sensitivity analysis, propensity scores were re-estimated by using two other cutoff values for converting the continuous cost variable to a dichotomous one. Applying a cutoff as low as the 25th percentile or as high as the 75th percentile did not appreciably change the propensity score distribution.

The covariates from all of the data dimensions were sorted together in descending order of their estimated multiplicative bias, and the top 500 were selected to be included in the propensity score analysis. Logistic regression was used to estimate the predicted probability of exposure to tiotropium conditional on all included covariates (i.e., propensity score). In addition to the 500 empirically selected covariates, we included an indicator variable for patient sex, categorical variables for age (in 5-year groupings), calendar year of treatment initiation, and categorical variables for patient Romano comorbidity score [16].

Average health-care system costs can be easily skewed by exceptionally ill patients to a degree that the average is not representative of any real patient. Furthermore, sicker patients are sometimes disproportionately channeled to newer treatments. To provide a more representative measure of cost, and to avoid biasing the analysis against the newer study drug (tiotropium), we estimated median costs instead of mean costs by using quantile regression. Quantile regression is similar to optimization-type regression on a data mean, but rather than finding the sample mean by minimizing the sum of squared residuals, as would be done in a conventional linear regression, the sample median is estimated by minimizing the sum of absolute residuals [17]. We used the Quantreg procedure in SAS (SAS Institute Inc., Cary, NC, USA) to perform the analysis on each outcome. We repeated the analysis on the 90th percentile of patients by cost (the most costly patients) and the 10th percentile of patients by cost (the least costly patients). The quantile regression models included a binary indicator variable for treatment assignment (=1 for tiotropium and =0 for ipratropium) and nine indicator variables for decile of propensity score.

Results

Between January 1, 2003, and December 31, 2006, 4,685 patients were started on tiotropium and 47,208 patients were started on ipratropium. Of these patients, 1,545 tiotropium patients and 21,026 ipratropium patients were excluded because they had either filled a prescription under British Columbia's provincial palliative care drug plan or long-term care drug plan, were of unknown age or sex, or were younger than 50 years of age at the time of their initial prescription. The final study population had 3,140 tiotropium patients and 26,182 ipratropium patients. Ninety-eight percent of patients in both treatment groups remained in the study for the entire 720-day follow-up period. Of patients who exited the study early, the median follow-up time was 495 days for tiotropium patients and 400 days for ipratropium patients.

Baseline characteristics of the study population are shown in Table 1. The average age of study participants was 68 years, and 53% of the patients were women. Ipratropium patients were more likely to be from lower income brackets. In terms of baseline health status, there were few notable differences between the treatment groups. The ipratropium group had more patients with a Romano score of zero (tiotropium: 26%; ipratropium: 40%), which indicates that these patients had no major diagnosed morbidities in the year prior to initial treatment. The tiotropium group had higher percentages of patients with asthma and COPD diagnoses but lower percentages of patients with diagnoses classified as other airway disease or respiratory infection. The characteristics of a propensity-score–matched subset of the study population were balanced across treatment groups (Table 2) and were used to provide data on comparability of the two groups conditional on the propensity score.

We examined the 10th percentile, median, and 90th percentile of patients by total direct health-care cost (Table 3). In our propensity-score–adjusted study population, there was no evidence that patients started on tiotropium incurred lower health-care costs than did patients started on ipratropium in the first 2 years after initiating treatment. There was a clear total cost disadvantage of tiotropium over ipratropium across all eight quarters for both the median and 10th percentile, with quarterly cost differences typically occurring in the Can $50 to Can $100 range per patient. In the 90th percentile of patients, the most expensive patients in terms of health-care costs, the estimated differences in cost were less apparent. Although point estimates in six of eight quarters favored ipratropium, differences were not statistically significant in seven of eight quarters, and no drug clearly appeared to be superior to the other. Median differences in total cost by quarter are plotted in Figure 1. In addition to median total direct costs for tiotropium patients exceeding those for ipratropium patients in all quarters, there was a significant trend in increased median cost differences over time ($b = 6.5$ per quarter; $P = 0.01$).

Median cost differences for prescription drugs and physician visits are shown in Table 4. With the exception of the first 90 days after treatment initiation, physician visit costs did not differ significantly between study arms. Median prescription drug costs, which included the cost of the study drugs, were typically Can $75 to Can $95 greater in all quarters of follow-up in patients who initiated treatment with tiotropium. Median cost differences for hospitalizations were zero because a majority of patients in the first 2 years of follow-up were not admitted to hospital. Differences in average hospital costs were not statistically significant in any quarter. Chronologically, those average costs per patient per quarter were as follows (95% confidence intervals in parentheses): −39 (−249 to 170), −85 (−345 to 176), −41 (−195 to 114), −67 (−248 to 115), −21 (−181 to 140), 78 (−103 to 258), 69 (−96 to 235), and −121 (−296 to 53).

Discussion

Varying results from previous studies on the benefits of tiotropium prevented us from having a strong a priori expectation for the results of this analysis. It was plausible that direct health-care costs would possibly be lower for patients initially treated with tiotropium, both because some studies found reductions in hospitalizations with tiotropium and also because a convenience advantage over ipratropium could have improved treatment persistence. What we observed were statistically significantly higher costs in patients who started on tiotropium instead of ipratropium in the median and 10th quartile of patients by cost. The magnitude of these increases was compara-

Table 1 – Baseline characteristics of the study population.

Characteristic	Ipratropium		Tiotropium	
	n	%	n	%
Patients	26,182		3,140	
Age (y)				
50–54	2,727	10	229	7
55–59	3,561	14	387	12
60–64	3,856	15	500	16
65–69	4,087	16	551	18
70–74	4,365	17	529	17
75–79	3,862	15	482	15
80–84	2,433	9	301	10
85+	1,291	5	161	5
Sex				
Women	13,925	53	1,593	51
Men	12,257	47	1,547	49
Income band* (Can $)				
0–25,000	7,359	28	629	20
25,001–50,000	6,368	24	907	29
50,001–100,000	4,039	15	872	28
100,000 +	892	3	228	7
Non–income-based plan	2,900	11	55	2
Unregistered	4,624	18	449	14
Romano score†				
0	10,365	40	806	26
1–2	13,227	51	1,959	62
3–4	2,244	9	340	11
5+	346	1	35	1
Diagnoses between in previous 365 d				
Asthma (ICD493)‡	4,762	18	994	32
COPD (ICD490-492, 494-496)	7,578	29	1,579	50
Other airway disease (ICD466, 480-486, 7700)	6,959	27	795	25
Respiratory infection (ICD460-465)	5,218	20	597	19
Hospital discharges in previous 365 days				
1	5,974	23	664	21
2	2,425	9	216	7
>2	1,655	6	109	3
Median number of prescriptions in previous 365 d	19		20	
Hospital costs (Can $)	10,990		5,887	
Prescription costs (Can $)	1,509		1,794	
Physician visit costs (Can $)	1,563		1,424	
2003 Qtr 1	1,826	7	70	2
2003 Qtr 2	1,633	6	207	7
2003 Qtr 3	1,241	5	142	5
2003 Qtr 4	1,927	7	197	6
2004 Qtr 1	1,880	7	156	5
2004 Qtr 2	1,495	6	180	6
2004 Qtr 3	1,216	5	144	5
Calendar year of index dispensing				
2004 Qtr 4	1,772	7	219	7
2005 Qtr 1	1,996	8	205	7
2005 Qtr 2	1,645	6	218	7
2005 Qtr 3	1,323	5	217	7
2005 Qtr 4	1,654	6	226	7
2006 Qtr 1	1,999	8	233	7
2006 Qtr 2	1,669	6	264	8
2006 Qtr 3	1,319	5	205	7
2006 Qtr 4	1,587	6	257	8

COPD, chronic obstructive pulmonary disease.

* Author-defined groupings of Fair PharmaCare income-based drug plans. These groupings combine Fair PharmaCare Regular Assistance (nonseniors) and Enhanced Assistance (seniors) plans.

† The Romano score is a diagnosis-based score derived from the Charlson index of 19 conditions; each has a weight from 1 to 6. The score for each patient is equal to the sum of the weights.

‡ The International Classification of Diseases, Ninth Revision (ICD-9).

Table 2 – Baseline characteristics of a propensity-score–matched subset of the study population.

Characteristic	Ipratropium		Tiotropium	
	n	%	n	%
Patients	3,076		3,076	
Age (y)				
50–54	253	8	229	7
55–59	350	11	377	12
60–64	460	15	489	16
65–69	576	19	535	17
70–74	489	16	520	17
75–79	465	15	468	15
80–84	309	10	298	10
85+	174	6	160	5
Sex				
Women	1,585	52	1,562	51
Men	1,491	48	1,514	49
Income band* (Can $)				
0–25,000	625	20	624	20
25,001–50,000	877	29	892	29
50,001–100,000	851	28	842	27
100,000+	215	7	216	7
Non–income-based plan	65	2	55	2
Unregistered	443	14	447	15
Romano score†				
0	768	25	803	26
1–2	1,950	63	1,910	62
3–4	322	10	330	11
5+	36	1	33	1
Diagnoses between in previous 365 d				
Asthma (ICD493)‡	982	32	957	31
COPD (ICD490-492, 494-496)	1,447	47	1,528	50
Other airway disease (ICD466, 480-486, 7700)	821	27	775	25
Respiratory infection (ICD460-465)	606	20	583	19
Hospital discharges in previous 365 d				
1	647	21	649	21
2	229	7	214	7
2	117	4	108	4
Median number of prescriptions in previous 365 d	21		20	
Hospital costs (Can $)	6,138		5,963	
Prescription costs (Can $)	1,681		1,659	
Physician visit costs (Can $)	1,436		1,420	
2003 Qtr 1	136	4	70	2
2003 Qtr 2	137	4	205	7
2003 Qtr 3	118	4	140	5
2003 Qtr 4	181	6	195	6
2004 Qtr 1	201	7	152	5
2004 Qtr 2	166	5	179	6
2004 Qtr 3	141	5	144	5
Calendar year of index dispensing				
2004 Qtr 4	208	7	212	7
2005 Qtr 1	244	8	195	6
2005 Qtr 2	206	7	215	7
2005 Qtr 3	174	6	216	7
2005 Qtr 4	233	8	221	7
2006 Qtr 1	280	9	229	7
2006 Qtr 2	258	8	259	8
2006 Qtr 3	167	5	197	6
2006 Qtr 4	226	7	247	8

COPD, chronic obstructive pulmonary disease.

* Author-defined groupings of Fair PharmaCare income-based drug plans. These groupings combine Fair PharmaCare Regular Assistance (nonseniors) and Enhanced Assistance (seniors) plans.

† The Romano score is a diagnosis-based score derived from the Charlson index of 19 conditions; each has a weight from 1 to 6. The score for each patient is equal to the sum of the weights.

‡ *The International Classification of Diseases, Ninth Revision* (ICD-9).

Table 3 – Total direct costs* per patient over 720 days for 3,140 tiotropium and 28,162 ipratropium patients.

Quantile	Quarter (+ cost difference favors ipratropium/− cost difference favors tiotropium)							
	1	2	3	4	5	6	7	8
10th Quantile (Lowest Cost Patients)								
Tiotropium	114	96	94	102	121	105	102	114
Ipratropium	76	44	41	46	61	49	45	51
Difference†	38	52	53	56	60	55	57	62
L95% C.I.	21	34	33	34	39	34	34	43
U95% C.I.	55	70	73	78	82	76	80	82
Median (Typical Cost Patients)								
Tiotropium	557	563	549	576	619	608	629	638
Ipratropium	512	487	472	495	513	514	533	540
Difference†	45	76	77	81	106	94	96	98
L95% C.I.	12	49	49	50	77	66	65	63
U95% C.I.	78	103	105	112	135	123	127	134
90th Quantile (Highest Cost Patients)								
Tiotropium	1880	2170	1787	1951	1935	2216	2211	2251
Ipratropium	2136	1976	1820	1906	1930	1974	2123	2168
Difference†	−255	194	−33	45	5	242	88	83
L95% C.I.	−535	2	−198	−175	−220	−61	−174	−147
U95% C.I.	25	385	131	265	230	545	350	313

* Costs are indicated in Canadian dollars per patient (1 dollar CAD equals approximately 1 dollar USD). Components included in total direct cost include hospital costs, physician visit costs and prescription drug costs.

† L95% C.I. and U95% C.I. denote the lower 95% and upper 95% confidence interval for the difference between tiotropium and Ipratoprium.

ble to the price difference between the two drugs. We did not observe any significant differences when we analyzed the physician visit and hospitalization costs separately. These results suggest that tiotropium patients were more costly at least in part due to the higher cost of their medication. Tiotropium also did not appear to provide a health-care cost advantage in the most costly patients (at the 90th percentile). Significantly higher costs in tiotropium patients in the second and sixth quarters of follow-up were not sufficiently compelling to conclude, in our study population, that ipratropium was advantageous in higher cost patients.

Although we controlled for calendar year of initiation on treatment, we observed a significant trend over time toward an increase in median cost differences between tiotropium and ipratropium patients. The reasons for this result are not immediately obvious. At 28%, overall spending on health care in British Columbia increased rapidly over the study period [18]. It is reasonable that annual global increases of approximately 5% in health-care funding would be applied equally to patients in both treatment groups, but if one group was more expensive than the other, an identical multiplicative increase of 5% per year on average would translate into larger absolute differences over time. Another possible reason for the trend could be differences in treatment persistence on the two drugs in some patients. Tiotropium has a convenience advantage and a drug cost disadvantage compared with ipratropium. The former could improve drug persistence in some patients and therefore increase drug costs. The latter could reduce drug persistence in some patients and possibly increase health-care costs because of suboptimal disease control. Yet another possible explanation can be derived from previous studies that found an increase in hospitalizations in tiotropium patients [13,14]. If tiotropium actually increases the risk of hospitalization compared with ipratropium, then it is reasonable to expect that such added risk would also increase health-care costs. This analysis, however, cannot be taken as direct evidence of any of the above effects.

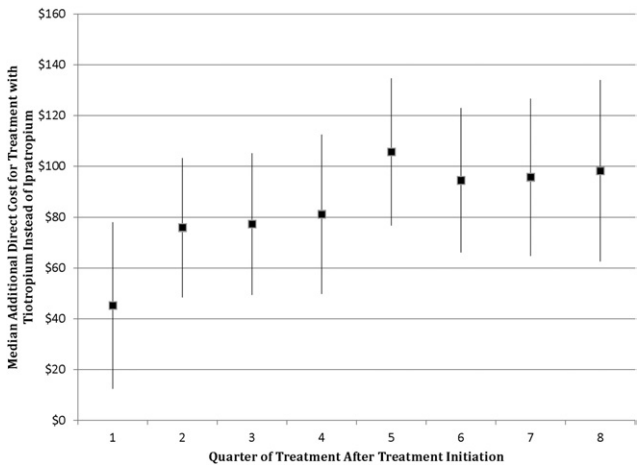

Fig. 1 – Difference in median direct health care cost per patient treated with tiotropium or ipratropium.

Our study had some limitations. With any observational study there can be no guarantee that the analysis is immune to bias from confounding factors. The hdPS method employed a rigorous and systematic approach to adjustment for confounding. Data on a matched subset of patients demonstrated that tiotropium and ipratropium patients were comparable on observed characteristics conditional on their propensity score, including cost in the year prior to drug initiation (Table 2). This feature of the analysis provided some assurance that the hdPS method provided adjustment for confounding, at least for measurable factors. Unmeasured confounding could still have been

Table 4 – Direct costs* per patient for 3,140 tiotropium and 28,162 ipratropium patients, by system component.

Median cost†	Quarter (+ difference favors ipratropium/− difference favors tiotropium)							
	1	2	3	4	5	6	7	8
Physician Visits								
Tiotropium	200	159	162	167	165	175	182	175
Ipratropium	216	167	160	167	167	168	170	168
Difference‡	−16	−8	3	0	−1	7	12	7
L95% C.I.	−30	−21	−9	−12	−14	−4	−2	−8
U95% C.I.	−3	5	15	12	12	19	25	22
Prescription Drugs								
Tiotropium	295	340	320	337	365	361	356	376
Ipratropium	215	245	242	262	272	272	277	282
Difference‡	80	95	78	75	93	89	79	95
L95% C.I.	63	75	59	53	72	69	58	69
U95% C.I.	98	115	97	98	114	110	101	120

* Costs are indicated in Canadian dollars per patient (1 dollar CAD equals approximately 1 dollar USD).

† Median hospital costs were zero in all time periods. Average cost difference between treatment group for hospitalizations were, by quarter (95% confidence intervals in brackets): −39 (−249, 170), −85 (−345, 176), −41 (−195, 114), −67 (−248, 115), −21 (−181, 140), 78 (−103, 258), 69 (−96, 235), −121 (−296, 53).

‡ L95% C.I. and U95% C.I. denote the lower 95% and upper 95% confidence interval for the difference between tiotropium and Ipratoprium.

a factor in the analysis. For example, tiotropium was a new drug during the study period and it is possible that higher risk patients were preferentially channeled toward tiotropium rather than ipratropium. Our use of administrative claims data for diagnoses, medical procedures, and drug use may not have captured all relevant information on health status, and to the extent that important data were lacking in the analysis, our results could have been biased. Different results may also have been obtained if other nonsystem costs were included. Finally, our analysis provided useful information on the relative costs of two active treatments, but it did not offer any information on whether treatment with tiotropium or ipratropium is preferable to treatment with other inhaled medications, or no IAC whatsoever.

The cost structure of health-care services in British Columbia is also somewhat unique, and the absolute cost differences we observed are not necessarily generalizable to other jurisdictions. This is less of a concern for hospital costs and physician costs where we did not find evidence of a difference. Jurisdictional uniqueness is most relevant to the cost difference between ipratropium and tiotropium in that the advantage of ipratropium would be comparatively greater in jurisdictions where the price difference with tiotropium was larger, and comparatively less where the price difference was smaller.

This study did not provide support for preferential use of tiotropium over ipratropium with regard to direct health-care costs. Health plans that pay for tiotropium in anticipation of cost savings on hospital and physician services may wish to reconsider their tiotropium policies with respect to patients with COPD and determine whether coverage remains warranted on the basis of added convenience or other real or perceived advantages of the drug.

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