

The potential economic impact of restricted access to angiotensin-receptor blockers

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ABSTRACT

Background: The use of angiotensin-receptor blockers increased by more than 4000% in Canada from 1996 to 2006. The benefit of these medications over angiotensin-converting-enzyme (ACE) inhibitors has not been proven aside from a reduction in dry cough. We estimated the potential cost savings that might have been achieved had access to angiotensin-receptor blockers been restricted.

Methods: We performed a cost-minimization analysis with a decision-tree model using a societal perspective over a one-year period. Sources of data for model parameters included IMS Health Canada data collected from one-third of all retail pharmacies for the cost and use of angiotensin-receptor blockers and ACE inhibitors in each province, as well as published studies for administrative costs and incidence

of dry cough. We used Monte Carlo simulations with 10 000 iterations to test the impact of several model parameters (e.g., drug prices, administrative costs and the incidence of dry cough). All data are in 2006 Canadian dollars.

Results: A policy that would have restricted access to angiotensin-receptor blockers might have saved more than \$77 million in Canada in 2006. The simulations yielded similar savings for the year (mean \$58.3 million, 95% confidence interval \$29.3 million to \$90.8 million). Every simulation showed a cost savings.

Interpretation: Had access to angiotensin-receptor blockers been restricted, the potential cost savings to the Canadian health care system might have been more than \$77 million in 2006, likely without any adverse effect on cardiovascular health.

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Costs of cardiovascular drugs in Canada increased by more than 200% from 1996 to 2006. The use of angiotensin-receptor blockers grew at an especially high rate, rising by more than 4000% during that period.¹ Such an increase in the use of these agents is not strongly supported by evidence.¹ Although angiotensin-receptor blockers were effective in reducing mortality and morbidity associated with hypertension in one large trial, patients in the control group were not given an angiotensin-converting-enzyme (ACE) inhibitor.² Instead, they received atenolol, a β -blocker, a drug class whose use is increasingly being questioned in the management of high blood pressure uncomplicated by prior myocardial infarction, heart failure or tachyarrhythmia.^{3,4} Although angiotensin-receptor blockers are not associated with dry cough, a side effect reported by 5%–35% of patients taking ACE inhibitors,⁵ this side effect is benign and fully reversible once the drug is stopped. Meta-analyses that included several randomized trials failed to show superiority of angiotensin-receptor blockers over ACE inhibitors for the treatment of hypertension,⁶ heart

failure⁷ or the secondary prevention of coronary artery disease.⁸

Innovative policies are needed to offset the ever-increasing costs of cardiovascular drugs in Canada. Currently, British Columbia is the only province that restricts access to angiotensin-receptor blockers. Given that these agents can safely be substituted by ACE inhibitors and still yield similar clinical outcomes,^{6–8} restricting their access is expected to lead to cost savings without adversely affecting patient health. We estimated the potential cost savings that might have been achieved had access to angiotensin-receptor blockers been restricted in Canada in 2006.

Methods

Study design

We conducted a cost-minimization economic analysis using a decision-tree model with province-level data on drug costs obtained from IMS Health Canada's Canadian CompuScript Audit Database.¹⁹ We built the model to perform our base-case analysis and sensitivity analyses over a

one-year period from a societal perspective (Figure 1). Using the model, we compared direct health care costs in 2006 associated with two scenarios. The first scenario reflected the status quo of no restriction on the use of angiotensin-receptor blockers across Canada except in British Columbia. Actual 2006 data on costs were used.

The second scenario tested the economic outcomes had a policy restricting the use of angiotensin-receptor blockers been implemented on Jan. 1, 2006. We assumed that patients would receive treatment for one year. Under this policy, those already taking an angiotensin-receptor blocker or an ACE inhibitor would continue taking their existing therapy for the duration of the year. New patients considered for angiotensin-modifying treatment would be prescribed an ACE inhibitor first. We assumed that constraints on the use of angiotensin-receptor blockers would be more acceptable if the initially prescribed ACE inhibitor was not one that required multiple doses per day (e.g., captopril and enalapril). Patients already receiving these ACE inhibitors, however, would not be switched to another regimen. New patients prescribed any of the other ACE inhibitors would be switched to an angiotensin-receptor blocker after the first month if dry cough developed.

In modelling the restriction-policy arm, we used province-level data on market share for the ACE inhibitors that did not require multiple daily doses. Using these data to determine the proportion of patients prescribed each ACE inhibitor as first-line treatment would tend to favour newer, and possibly more effective, agents.¹⁰ Finally, we assumed no restriction on angiotensin-receptor blockers within the class, with prescription rates

of each agent based on provincial market share data for each drug in 2006.

Estimation of drug use and costs

Actual 2006 data on market shares and monthly costs for angiotensin-receptor blockers and ACE inhibitors were extracted from IMS Health Canada's Canadian CompuScript Audit Database for all provinces. This database uses audits at the retail pharmacy level to estimate the number and value of prescriptions dispensed throughout Canada. Pharmacy outlets are stratified by region, type of retailer (independent or chain store) and size. Sample stores selected for audit represent about one-third of all retail pharmacies. Data for the audit are collected monthly by electronic means. After passing through various quality-control verifications, the sample data are projected to the total group of pharmacies in each region; regional totals are then summed to provide a national estimate. The data collected can be used to determine product use by drug class as well as costs of the prescriptions as dispensed (including all mark-ups and pharmacists' fees).

For our study, we included data from Jan. 1, 2005, to Dec. 31, 2006. IMS Health Canada does not measure population-wide, patient-specific data. Since we could not obtain patient-level costs, we extrapolated monthly average dispensation costs at a provincial level from the IMS Health Canada database.

Switching from an ACE inhibitor to an angiotensin-receptor blocker was assumed to be associated with additional physician consultation fees and administrative costs. We extracted physician fees from each province's physician's manual on fee schedules.¹¹⁻¹⁸ Administrative fees were based on those associated with reference pricing for

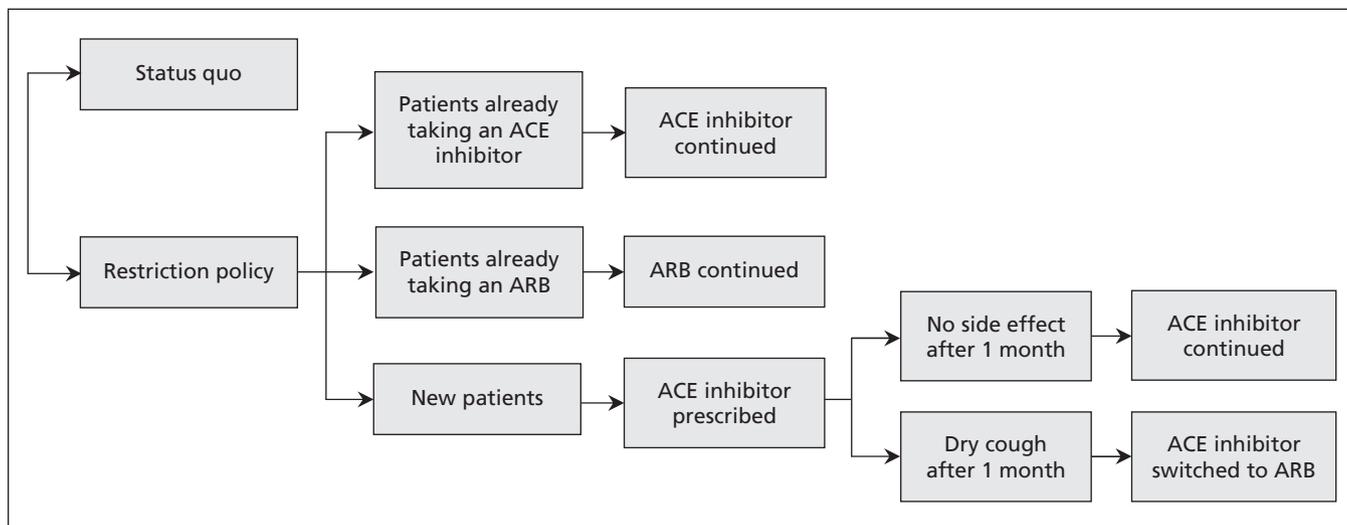


Figure 1: Decision-tree model used to compare the potential cost savings of a hypothetical policy of restricted access to angiotensin-receptor blockers and the status quo in 2006. Note: ACE = angiotensin-converting enzyme, ARB = angiotensin-receptor blocker.

ACE inhibitors in British Columbia as reported by Schneeweiss and colleagues¹⁹ and were actualized to 2006 values using the Consumer Price Index for health care in 2006. To be conservative, in the Quebec model, we assumed that a pharmacist consultation fee would be required in addition to a physician fee.²⁰

Estimation of drug effectiveness and side effects

We assumed that selected ACE inhibitors and angiotensin-receptor blockers were of equivalent effectiveness within their respective drug classes for every possible indication.⁶⁻⁸ This assumption was fundamental for the validity of our cost-minimization analysis.

From the available Canadian pharmacoepidemiologic data, we determined that 9.2% of patients prescribed an ACE inhibitor later switched to an angiotensin-receptor blocker within one year. We used this switch rate as the base-case value for the incidence of dry cough, acknowledging that switches might not be all related to this side effect of ACE inhibitor use. Angiotensin-receptor blockers were assumed to be free of side effects.

Statistical analysis

Because of variability in drug costs and utilization rates between provinces, we analyzed data for each province separately except those for Newfoundland and Labrador and for Prince

Edward Island, which we analyzed together because of how they were provided by IMS Health Canada. The savings of the restriction policy are presented in total absolute savings and relative savings. Given the short-term perspective of our analysis, no discounting was applied. To test the robustness of the base-case analysis, we used Monte Carlo simulations with 10 000 iterations to estimate the impact of several model parameters. The parameters included drug costs, incidence of dry cough, new-to-existing patient ratios, number of patients affected by the restriction policy and administrative costs associated with switching from an ACE inhibitor to an angiotensin-receptor blocker.

One-way sensitivity analyses were performed to assess the impact of each model parameter on cost savings. In a final sensitivity analysis, we examined the impact of British Columbia's drug utilization ratios for new and existing patients in 2006 on each provincial model. We also applied data on British Columbia's market shares for ACE inhibitors and angiotensin-receptor blockers to each provincial model.

Results

Parameter estimates

Table 1 indicates base-case values for each parameter of interest as well as the plausible range and distribution used in the Monte Carlo simulations. Before 2006, about one-fourth of prescrip-

Table 1: Estimated values in 2006 for parameters used in the base-case model and sensitivity analyses

Parameter	Base case	Variation	Distribution
Monthly drug cost,* \$			
ACE inhibitors	11 190 031\$	10 981 042–11 308 802\$	Market share¶
Angiotensin-receptor blockers	16 109 865\$	16 073 648–16 199 335\$	Market share¶
% of patients already taking an ACE inhibitor	46.0\$	± 10	Uniform
% of patients already taking an angiotensin-receptor blocker	23.2\$	± 10	Uniform
No. of patients prescribed either medication in 2006	266 212\$	± 25%	Uniform
Incidence of dry cough, %	9.2	5–35	Uniform
Pharmacist fee†‡	\$17.59	NA	NA
Physician fee‡	\$58.94\$	NA	NA
Administrative fee‡	\$7.83	± 25%	Uniform

Note: ACE = angiotensin-converting enzyme, NA = not applicable.
 *Costs for ACE inhibitors and angiotensin-receptor blockers were derived from IMS Health Canada data and applied to the model independently of the number of patients receiving either agent in 2006.
 †The pharmacist fee was added only to the Quebec model.
 ‡Cost per patient who required a switch from an ACE inhibitor to an angiotensin-receptor blocker.
 §Mean national values. Each provincial model used associated provincial values.
 ¶Distribution is based on data provided by IMS Health Canada on the market share of each agent at the provincial level. The distributions inferred the projected costs for each province had their relative market share been one of the eight observed provincial relative market shares in Canada in 2006.

tions targeting the renin-angiotensin system were for an angiotensin-receptor blocker, and we assumed that these patients would continue to take their angiotensin-receptor blocker in 2006. We assumed that an administrative fee of \$7.83 would be applied for the evaluation of each authorization demand to switch to an angiotensin-receptor blocker as a result of dry cough from ACE inhibitor use.

Actual drug use and costs

Actual utilization rates and costs per month for each ACE inhibitor and angiotensin-receptor blocker in 2006 are shown in Table 2. The most frequently dispensed ACE inhibitors were ramipril and lisinopril. Of the angiotensin-receptor blockers, the most frequently prescribed agents were valsartan and irbesartan.

Potential cost savings with restricted access

Results of the base-case model show that a policy of restricted access to angiotensin-receptor blockers might have saved \$77.1 million overall in 2006 (Table 3); this value represents 5.6% of the total expenditures for angiotensin-receptor blockers and ACE inhibitors. Results also show potential cost savings in every province.

Table 4 shows the results of the Monte Carlo simulations for absolute and relative potential

savings by province. The total absolute savings (mean \$58.3 million, 95% confidence interval \$29.3 million to \$90.8 million) support the results of the base-case analysis. Every simulation showed a cost savings in every province.

Sensitivity analyses

In the one-way sensitivity analyses of the impact of model parameters on cost savings, only a handful of highly unlikely circumstances would have changed the direction of the results: the incidence of dry cough or the rate of switching from an ACE inhibitor to an angiotensin-receptor blocker would have to surpass 58%; the percentage of patients already taking an angiotensin-receptor blocker would have to exceed 43% (reducing the proportion of new patients affected by the restriction policy to 11%); or the administrative fees associated with switching to an angiotensin-receptor blocker would have to be more than \$1738 per prescription reviewed.

In one of the sensitivity analyses, we tested the effect of generic versions of patented drugs on potential savings. Because the most frequently prescribed medications will be off patent by 2011,²¹ we analyzed the effect of the restriction policy in a 2012 setting. We assumed that the price of patented drugs in 2006 that were going off patent before Jan. 1, 2012 (lisinopril, enalapril, fosinopril, eprosartan, ramipril, candesartan, irbesartan and valsartan), would be halved (based on recent legislation in Ontario limiting generic drug reimbursement to 50% of the cost of the brand name drug). All other parameters were kept at their base-case values. This analysis showed a cost saving in every province and a total potential saving across Canada of \$19.9 million (2.3% relative savings compared to the total cost of ACE inhibitors and angiotensin-receptor blockers).

In the sensitivity analysis of the impact of British Columbia's existing-to-new patient ratios and market shares on each provincial model, the results were similar to those of the base-case analysis, with a potential savings of \$85 million.

Interpretation

Our analyses showed that, had a policy restricting access to angiotensin-receptor blockers been implemented in Canada in 2006, the cost savings that year might have been \$77.1 million, likely without any adverse effect on health outcomes. A restrictive policy is currently in place in the province of British Columbia. In one of our sensitivity analyses, in which we used the same market shares observed in British Columbia in

Table 2: Actual data on market shares and monthly utilization rates and costs for ACE inhibitors and angiotensin-receptor blockers in 2006

Medication	% of national market share	No. of prescriptions per month	Cost per month, \$
ACE inhibitor			
Ramipril	51.3	746 513	488 839 477
Enalapril	15.7	163 337	149 250 024
Lisinopril	9.9	166 824	94 627 578
Perindopril	7.4	119 807	70 433 169
Quinapril	7.0	110 458	66 967 011
Fosinopril	3.9	78 762	37 537 172
Cilazapril	2.4	44 457	23 034 690
Trandolapril	1.5	25 277	14 416 529
Angiotensin-receptor blocker			
Irbesartan	24.5	133 034	149 222 836
Valsartan	24.2	97 636	147 348 843
Candesartan	19.2	70 965	116 876 630
Losartan	19.1	72 734	116 112 387
Telmisartan	11.8	53 285	71 741 136
Eprosartan	1.2	5 950	7 259 310

Note: ACE = angiotensin-converting enzyme.

2006, we found that the potential savings of \$85 million was similar to the savings projected in the base-case analysis.

Administrators of drug benefit plans need to consider carefully the restriction of specific drugs, let alone an entire class, especially in the absence of an effective alternative. In Quebec and Ontario, restricted access to clopidogrel led to underuse and increased mortality.^{22,23} However, in the case of angiotensin-receptor blockers, restricted access can result in substantial savings without leading to underuse or adverse clinical outcomes. In Sweden, reimbursement restrictions for angiotensin-receptor blockers were implemented in 2008. Since then, the proportion of the Swedish population dispensed an angiotensin-receptor blocker decreased by 24% in favour of other drugs and led to a decrease of close to 5% in total drug expenditures.²⁴

Other simple ways to save money have been proposed, such as switching from a thiazide diuretic plus either an ACE inhibitor or an angiotensin-receptor blocker to a single combination product. Such a strategy could potentially save up to \$45 million, again without any adverse effect on cardiovascular health and likely with a favourable impact on drug adherence.²⁵ Given a future of increasing economic uncertainty complicated by a demographic shift to an older population with a relatively shrinking tax base, measures are needed to deal with the rising health care costs.²⁶ Policies can neither be draconian nor take a one-size-fits-all approach. Patient well-being must always come first. Cost-sharing strategies such as co-payments or caps are a less satisfactory solution to the increasing costs of cardiovascular medications, because they shift the financial burden to patients and may lead to underuse and adverse clinical outcomes.²⁷

We believe that, where treatment choice exists, favouring the least expensive medication over others of comparable effectiveness is one way to address future economic challenges without creating social disparities.

Limitations

Our study has limitations. First, we did not assess clinical outcomes because we were unable to obtain patient-level information. The assumption of equivalent outcomes with ACE inhibitors and angiotensin-receptor blockers may not be true in Canada, although this is extremely unlikely based on the bulk of evidence. In addition, we considered that all selected drugs were equivalent for every possible indication; however, there is still debate on the actual equivalence of these drugs.

Second, we considered only direct medical

costs despite the societal perspective of our analysis. Costs not related to health care are likely negligible compared with the overall economic benefits of the policy.

Third, although side effects other than dry cough are known to be associated with ACE inhibitors,²⁸ we limited our analysis to dry cough.

Finally, the short timeline of our base-case analysis ignores the effect of future generic and cheaper angiotensin-receptor blockers. However, as seen in our projected sensitivity analysis of the effect of brand name drugs going off patent in 2012, the policy of restricted access would still result in cost savings, although to a lesser degree (\$19.9 million v. \$77.1 million).

Table 3: Potential cost savings in one year with a policy restricting access to angiotensin-receptor blockers (base-case model)

Province*	Absolute savings, \$ millionst	Relative savings, %
Alberta	9.5	6.4
Saskatchewan	3.2	6.7
Manitoba	4.5	8.8
Ontario	32.9	5.4
Quebec	18.3	4.7
New Brunswick	2.5	5.8
Nova Scotia	4.1	7.1
Newfoundland and Labrador, and Prince Edward Island	2.1	5.9
Total	77.1	5.6

*British Columbia is excluded from the model because it already has a restrictive policy for this drug class.
†Amounts are in 2006 Canadian dollars.

Table 4: Potential cost savings in one year with a policy restricting access to angiotensin-receptor blockers (Monte Carlo simulations)

Province*	Absolute savings, \$ millions (95% CI)†	Relative savings, % (95% CI)
Alberta	7.3 (4.0–11.1)	4.9 (2.7–7.5)
Saskatchewan	2.4 (1.3–3.6)	5.0 (2.7–7.5)
Manitoba	3.4 (2.1–4.9)	6.7 (4.2–9.6)
Ontario	25.4 (12.8–39.4)	4.2 (2.1–6.4)
Quebec	12.9 (5.0–21.6)	3.3 (1.3–5.6)
New Brunswick	2.0 (1.2–3.0)	4.7 (2.8–7.0)
Nova Scotia	3.4 (2.2–4.8)	6.0 (3.9–8.4)
Newfoundland and Labrador, and Prince Edward Island	1.4 (0.6–2.3)	3.8 (1.6–6.4)
Total	58.3 (29.3–90.7)	4.2 (2.1–6.6)

Note: CI = confidence interval.
*British Columbia is excluded from the model because it already has a restrictive policy for this drug class.
†Amounts are in 2006 Canadian dollars.

Conclusion

A policy of restricted access to angiotensin-receptor blockers might have saved the Canadian health care system \$77.1 million in 2006, likely without any adverse effect on cardiovascular health. Such strategies need to be considered in order to contain the steadily increasing costs of cardiovascular care.

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