Impact of Restrictive Prescription Plans on Heart Failure Medication Use

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Background—Prescription plans frequently use restrictive strategies to control drug expenditures. Increased restrictions may reduce access to evidence-based therapy among patients with chronic disease. We sought to evaluate the impact of increased restrictions on medication use among heart failure (HF) patients.

Methods and Results—We conducted a population-based cohort study of administrative data from 3 Canadian provinces. During 1998 to 2001, Quebec (QC) had a minimally restrictive plan, whereas Ontario (ON) and British Columbia (BC) had more restrictive prescription plans. We evaluated drug use at 30 days of discharge stratified by prescription plan. Provincial rates of filled prescriptions for HF drugs in QC, ON, and BC were 62%, 58%, and 47% for angiotensin-converting enzyme inhibitors; 34%, 22%, and 16% for β-blockers; 9%, 5%, and 3% for angiotensin receptor blockers; and 79%, 76%, and 62% for loop diuretics, respectively. In multivariate analyses, patients residing in provinces with restrictive plans were less likely to be prescribed drugs that were restricted, such as β-blockers (odds ratio, 0.53; 95% CI, 0.46 to 0.60; 0.36, 0.29 to 0.44, for ON and BC, respectively) and angiotensin receptor blockers (0.50, 0.45 to 0.56; 0.38, 0.32 to 0.46, for ON and BC, respectively), than drugs with no restrictions, such as loop diuretics (0.81, 0.74 to 0.88; 0.40, 0.36 to 0.45, for ON and BC, respectively) and angiotensin-converting enzyme inhibitors (0.80, 0.75 to 0.86; 0.47, 0.43 to 0.52, for ON and BC, respectively).

Conclusion—Among HF patients, residing in a province with a more restrictive prescription plan may be associated with lower use of restricted HF medications over and above the expected regional differences in HF drug use across provinces. (Circ Cardiovasc Qual Outcomes. 2009;2:484-490.)

Key Words: heart failure ■ health policy ■ medication adherence

Despite the potential public health benefit of enhanced access to prescription drugs, burgeoning prescription drug costs have led to increasingly restrictive prescription plans in the United States and Canada. Such plans use a number of strategies to restrict the use of new or expensive drugs including cost sharing, formulary restrictions, prior authorization, and step-therapy requirements. These types of policies have been shown to be effective in cost-containment but have also been shown to have variable effects on quality of care and health outcomes.1–5 Many restrictive policies add significant administrative hurdles to the prescribing of restricted drugs, which can lead to the underuse of drugs in patients who could potentially benefit from their use.4,6,7 In a recent study of Medicare Part D formularies which evaluated coverage for 152 commonly used drugs in the United States, some plans were highly restrictive, providing coverage of less than 65% of drugs.8

Cardiovascular medications are frequently restricted by policy to contain costs and ensure appropriate drug use for common cardiovascular conditions (ie, hypertension). However, antihypertensive medications are also indicated in heart failure (HF) for afterload reduction and adrenergic blockade. HF patients may be particularly susceptible to restrictions in drug access because drug therapy represents the cornerstone of HF management. Despite the ongoing use of these restrictive drug policies, their effect on the use of evidence-based drug therapy has not been investigated in patients with HF.

In Canada, prescription drug plans are under the jurisdiction of the provincial governments and vary by province with different uses of restrictive policies.9 Among Canadian provincial prescriptions plans, Quebec (QC) has the least restrictive plan, which provides access to most commonly prescribed drugs, whereas both Ontario (ON) and British Columbia (BC) have a more restrictive prescription plan.10–12

Received July 17, 2008; accepted June 19, 2009.

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Circ Cardiovasc Qual Outcomes is available at http://circoutcomes.ahajournals.org

DOI: 10.1161/CIRCOUTCOMES.108.804351

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By comparing the rates of drug use and outcomes across provinces with disparate prescription plans, we sought to examine the association between prescription plans and medication use among HF patients.

**WHAT IS KNOWN**

- Restrictive prescription policies are frequently used to reduce use of medication and to limit drug costs.
- Restrictive policies can reduce access to evidence-based prescription drugs among patients with chronic disease.

**WHAT THE STUDY ADDS**

- Restrictive prescription policies may be associated with a reduction in the use of evidence-based prescription drugs among heart failure patients.
- Marked regional differences in care frequently exist and must be considered when evaluating the effect of regional policies.

### Methods

#### Study Population

Using encrypted provincial health insurance numbers, individual patient data from hospital discharge summary databases from QC (Med-Echo), ON, (Canadian Institute for Health Information database), and BC (BC patient hospitalization database) were linked to their respective physician and drug claim databases in each province (QC, Regie de l’Assurance Maladie du Quebec; ON, Ontario Health Insurance Plan and Ontario Drug Benefit; BC, Pharmacare). All patients >65 years of age who were discharged with a main discharge diagnosis of HF (International Classification of Diseases, 9th Revision, code 428.x) between January 1, 1998, and December 31, 2001, and who had not been admitted to hospital within the prior 3 years for a primary diagnosis of HF were included. The coding accuracy of primary and secondary discharge diagnoses for persons with cardiovascular disorders has been validated for these databases.\(^{13,14}\) Furthermore, the 428 code has been previously shown to be accurate for HF diagnosis with agreement with both Framingham HF score and clinical diagnosis.\(^{15,16}\) These databases have also been validated for the accuracy of prescription claims based on filled prescriptions.\(^ {14}\) The provincial prescription claims database captures 100% of outpatient prescriptions filled for patients >65 years of age as all patients in this age group are covered by their respective provincial plan. Hospitals in these provinces do not provide prescription drugs for use after discharge. The cohort was limited to patients over the age of 65 years, as data for medication use is only available for this age group. The 3-year wash-out period for a hospitalization for HF was used to ensure that groups were of comparable severity of illness. The first admission to hospital with a primary diagnosis of HF was considered the index admission.

Standardized exclusion criteria were defined and used across provinces.\(^{17}\) The following patients were excluded: (1) >105 years of age; (2) HF coded as an in-hospital complication; (3) patients discharged to long-term care institution, rehabilitation center, another province, or psychiatric institution were also excluded because of the lack of information on medication prescriptions; and (4) invalid health insurance number. Vital statistics for all patients were obtained from the Med-Echo and Regie de l’Assurance Maladie du Quebec databases for QC, from the ON Registered Persons Database in ON and the Death Registry of the BC Vital Statistics Agency in BC.

#### Provincial Prescription Plans

In Canada, each province is mandated by the federal government to provide prescription drug coverage for all individuals >65 years of age. These provincial plans cover >95% of the population >65 years of age. Each province administers the plan independently from the federal government and the other provinces. All aspects of the plan, including the formulary of covered drugs, and the need for any cost-containing strategies are determined at the provincial level. During 1998 to 2001, there were no restrictive policies in place for any HF medications in QC (a limited use policy did exist for carvedilol during the first year of the study). However, both ON and BC had restrictions on the use of certain β-blockers (BBs) (ie, bisoprolol and carvedilol) and all angiotensin receptor blockers (ARBs). In BC and ON, ARBs could only be used for specific clinical indications (ie, intolerance to angiotensin-converting enzyme inhibitors [ACE-I]), which required additional administrative paperwork by the prescribing physician. There were no restrictive policies for ACE-I in any of the 3 provinces. A reference-based pricing policy on ACE-I was in effect in BC, but we did not consider such a policy to be restrictive as a number of studies have shown that such policies do not limit appropriate use of prescription drugs and have not been associated with adverse outcomes.\(^{12}\) Lastly, loop diuretics were not affected by any specific policy in any of the 3 provinces (Table 1).

#### Clinical Characteristics and Comedications

Based on the clinical model for HF mortality developed by Lee et al,\(^ {18}\) data on the following covariates were obtained from the index admission: cardiovascular disease (including ischemic heart disease, peripheral vascular disease, and cerebrovascular disease), diabetes, hypertension, cardiac arrhythmia, liver disease, chronic renal failure, rheumatologic disease, chronic lung disease, and dementia. Data on the use of in-hospital procedures (angiography, angioplasty, and coronary artery bypass grafting) and length of stay were also obtained. Data on treating physician specialty (cardiologist, internist, general practitioner), unique hospital identifier, hospital type (academic or nonacademic), and calendar year of the index admission (to account for temporal trends) were also included as relevant covariates. In addition, prescription data on all HF medications were obtained, including ACE-I, ARB, BB, and loop diuretics.

#### Drug Use Across Provinces

The primary outcome was the use of drugs within 30 days of discharge (ACE-I, ARBs, BBs, loop diuretics) as a function of the provincial prescription plan. Province of residence was used as a proxy for the provincial prescription plan. Drug use was defined as a filled prescription within 30 days of discharge. Patients who did not receive a prescription within this time frame were considered to be nonusers for the duration of the study. The 30-day cut-off was selected as a number of studies have demonstrated that prescriptions
at discharge are both a measure of quality of care and are related to cardiovascular outcomes.\(^{19,20}\) In addition, most prescriptions are filled within the first few days after discharge, and discharge prescription status has a very high persistence over time with few changes in medication regimens occurring in the outpatient setting.\(^{9,21}\) Because of differences in prescribing patterns in BC, where prescriptions were filled later than in QC and ON, we repeated our analysis by extending the definition for drug use to prescriptions filled within 90 days after discharge to ensure that all intended prescriptions were captured. We also examined drugs not affected by policy—specifically, loop diuretics and ACE-I—as a measure of the underlying variability in HF drug use between provinces.

**Sensitivity Analysis**
To examine the robustness of our analysis, we performed a sensitivity analysis in which we limited our initial cohort to patients who were not receiving ACE-inhibitors within 30 days of discharge. Our objective was to determine the effect of restricting ARBs, an alternative medication choice for afterload reduction in this population. During the timeframe of our study, ARBs were restricted in BC and ON but not in QC. Use of loop diuretics was again used to gauge the underlying variability in HF drug use between provinces.

**Statistical Analysis**
Clinical characteristics across provinces were compared by the \(\chi^2\) test for categorical variables and by the Student \(t\) test for continuous variables. Because of the clustered data structure at the hospital level, we performed all analyses using generalized estimating equations with a logit link.\(^{22}\) Generalized estimating equations regression models compared HF drug use rates (ACE-I, ARBs, BB, and loop diuretics) as a function of province. Models were adjusted for age, sex, comorbidities, in-hospital interventions, length of stay, and characteristics of the treating physician (cardiologist, internist, or general practitioner) and hospital type (teaching, nonteaching). A unique hospital identifier was also entered into the model to account for within hospital correlations. Results are presented as odds ratios (ORs) and 95% CIs, with QC (the province with the least restrictive prescription plan) as the province of reference.

We considered that the effect of policy was significant only when the effect size (as measured by the upper limit of the CI for use of a given drug) was larger than the underlying variability in HF drug use between provinces, as gauged by the lower limit of the CI for ACE-I or loop diuretic use. In effect, we used unrestricted drugs (ACE-I and loop diuretics) as an estimate of the maximal confounding (ie, estimated using the minimum of the 2 lower limits of the CI for the unrestricted drugs should be equally prescribed across all provinces if the distribution of other factors influencing prescription across provinces were equal. Under this scenario, the OR for unrestricted drugs should be null when all covariates affecting prescription are controlled. Therefore, any deviation from the null for unrestricted drug is attributable to the net effect of unmeasured covariates on prescription use across provinces. This deviation can also be interpreted as a measure of the regional variation unexplained by the measured covariates. We operationalized this measure by using the minimum of the 2 lower limits of the CI for the unrestricted drugs as an estimate of the maximal confounding (ie, estimated using the confounding OR). If the CIs of the measure of effect of province did not overlap with this minimum lower CI limit, we considered that the effect of the restrictions on drug use was larger than would be expected from the net residual confounding (or unexplained regional variation).

**Results**

**Baseline Characteristics**
The study cohort comprising 67,040 patients discharged from hospital between 1998 and 2001, with a new diagnosis of HF. There were 29% (\(n=19,323\)), 16% (\(n=10,837\)) and 55% (\(n=36,880\)) from QC, BC, and ON, respectively. Mortality within 30 days from discharge for QC, BC, and ON was 3.3%, 4.5%, and 5.2%, respectively. Patients from QC were slightly younger but had a higher burden of comorbidities than patients from BC and ON (Table 2). Patients from QC also had higher rates of angiography (7%) and coronary revascularization (2%) and were also treated more frequently by a cardiologist (32%) than patients from BC and ON. Patients from BC were treated less often in teaching hospitals compared to patients in the other provinces.

**Use of HF Drugs**
For patients from QC, ON, and BC, ACE-I were prescribed within 30 days of discharge in 62%, 58%, and 47%; BBs in 34%, 22%, and 16%; ARBs in 9%, 5%, and 3%; and loop diuretics in 79%, 76%, and 62%, respectively (Figure 1). QC, the province with the least restrictive plan, had highest prescription rates of all HF drugs. In multivariate analyses, patients in BC and ON (ie, the provinces with more restrictive prescription plans) were less likely to be prescribed all studied HF drugs than patients in QC. Patients residing in provinces with restrictive plans were also much less likely to be prescribed restricted drugs, such as BBs (0.53, 0.46 to 0.60; 0.36, 0.29 to 0.44, for ON and BC, respectively) and ARBs (0.50, 0.45 to 0.56; 0.38, 0.32 to 0.46, for ON and BC, respectively) than patients residing in QC (Table 3). Within the BB drug class, drugs with restrictions (bisoprolol) were used much less frequently in ON and BC than drugs without restrictions (metoprolol; see Figure 2). We also found that the

### Table 2. Baseline Characteristics of HF Patients by Province

<table>
<thead>
<tr>
<th>Province</th>
<th>QC (n=19,323)</th>
<th>ON (n=36,880)</th>
<th>BC (n=10,837)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean±SD</td>
<td>78.3±7.4</td>
<td>79.0±7.6</td>
<td>79.2±7.3</td>
</tr>
<tr>
<td>Male, %</td>
<td>47</td>
<td>47</td>
<td>50</td>
</tr>
<tr>
<td>Median (IQR) length of stay, d</td>
<td>7 (4–12)</td>
<td>6 (3–9)</td>
<td>6 (4–10)</td>
</tr>
<tr>
<td>Comorbidities, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>32</td>
<td>25</td>
<td>22</td>
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<tr>
<td>Systemic hypertension</td>
<td>36</td>
<td>23</td>
<td>21</td>
</tr>
<tr>
<td>Atrial fibrillation and flutter</td>
<td>40</td>
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<td>24</td>
</tr>
<tr>
<td>Chronic obstructive lung disease</td>
<td>32</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>21</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>19</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
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<td>Peripheral vascular disease</td>
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<td>3</td>
</tr>
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<td>Malignancy</td>
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<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Dementia</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Procedures, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiography</td>
<td>7</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Admitting physician, %</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>General practitioner</td>
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<td>40</td>
<td>60</td>
</tr>
<tr>
<td>Cardiologist</td>
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<td>16</td>
<td>13</td>
</tr>
<tr>
<td>Internal medicine</td>
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<td>34</td>
<td>23</td>
</tr>
<tr>
<td>Hospital type: teaching</td>
<td>17</td>
<td>17</td>
<td>8</td>
</tr>
<tr>
<td>No. of hospitals</td>
<td>105</td>
<td>211</td>
<td>93</td>
</tr>
</tbody>
</table>

IQR indicates interquartile range, \(P<0.001\) for all covariates across provinces.
use of BBs such as atenolol and acebutolol, with little evidence for benefit in HF, were used relatively more frequently in BC and ON, than in QC. We also found that nonrestricted drugs were less frequently prescribed among patients residing in provinces with a restrictive plan. ORs for use of ACE-I were 0.80 (95% CI, 0.75 to 0.86) for ON and 0.47 (95% CI, 0.43 to 0.52) for BC. ORs for use of loop diuretics were 0.81 (95% CI, 0.74 to 0.88) for ON and 0.40 (95% CI, 0.36 to 0.45). All analyses of drug use were repeated using prescriptions within 90 days of discharge and showed similar results (data not shown).

### Effect of Policy Restrictions on Drug Use

To determine whether residence in a province with a restrictive plan affected the use of HF medications, we compared the ORs (and CIs) for the use of restricted drugs to nonrestricted drugs. When comparing with drug use in QC, a statistically significant association between policy restrictions and use of restricted HF medications was observed in ON for both ARBs and BBs as the ORs for restricted drugs was significantly smaller than the ORs for unrestricted drugs with no overlap of the CIs (minimum lower limit of the CI for the unrestricted drugs was 0.74 for ON). A similar trend was also seen for drugs affected by policy in BC but was not statistically significant (minimum lower limit of the CI for the unrestricted drugs was 0.36 for BC).

### ARB Use Among HF Patients Not Receiving ACE-I

To further explore the effect of restrictive policies on drug use and clinical outcomes, we examined a subset of HF patients who were not receiving ACE-I 30 days postdischarge. We evaluated the effect of a restrictive policy on ARB use among these patients. This subgroup of patients was selected to explore the effect of restricting an alternative HF therapy (ARB) among HF patients not receiving afterload reduction.

A total of 28,441 patients were discharged with a new diagnosis of HF and did not receive ACE-I within 30 days of discharge. Baseline characteristics for this subgroup are presented in Table 4. Among this subgroup of patients, the use of ARBs was highest in QC (21%), where there was no restrictive policy on ARB use, compared to ON (9%) and BC (6%), where such policy was in effect during the time of the study. Use of hydralazine was minimal in all 3 provinces (data not shown). In fully adjusted models, patients from provinces with ARB restrictions were significantly less likely to receive ARBs when compared to patients from provinces with no ARB restrictions (OR, 0.45; 95% CI, 0.40 to 0.51; OR, 0.32; 95% CI, 0.26 to 0.38, for ON and BC patients, respectively). Patients from provinces with a restrictive plan were also less likely to receive loop diuretic (OR, 0.68; 95% CI, 0.62 to 0.74; OR, 0.33; 95% CI, 0.29 to 0.36, for ON and BC patients, respectively). When comparing with drug use in QC, we found a significant association between ARB restriction and ARB use in Ontario as the OR for ARBs was significantly smaller than the OR for loop diuretics with no overlap of the CIs (lower limit for unrestricted drugs was 0.62 for ON).

### Discussion

Our study of 67,040 HF patients examined the effect of restrictive provincial prescription policies on the use of HF medications and outcomes among older HF patients. By comparing rates of drug use across 3 Canadian provinces with disparate prescription plans, we found that patients residing in ON, a province with a more restrictive prescription plan, were significantly less likely to receive HF medications including ACE-I, ARBs, and BBs. We also found that restricted drugs, such as ARBs and BB, were much less prescribed than drugs without restrictions in ON. A similar trend in drug use was also noted in BC, which also had a restrictive policy, but this did not reach statistical significance. Furthermore, when certain evidence-based BBs were restricted (ie, bisoprolol), we found higher prescription rates for atenolol and acebutolol, which have not been shown to be beneficial among HF patients in large randomized trials. We also specifically examined the effect of restricting ARB access on ARB use among patients not receiving ACE-I. We found that among

### Table 3. Crude and Adjusted ORs for Drug Use by Province Within 30 Days After Discharge

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ON</td>
<td>BC</td>
</tr>
<tr>
<td>ACE-I</td>
<td>0.87 (0.84–0.90)</td>
<td>0.56 (0.53–0.59)</td>
</tr>
<tr>
<td>BBs</td>
<td>0.56 (0.54–0.59)</td>
<td>0.36 (0.34–0.38)</td>
</tr>
<tr>
<td>ARBs</td>
<td>0.47 (0.44–0.50)</td>
<td>0.33 (0.30–0.37)</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>0.84 (0.81–0.88)</td>
<td>0.43 (0.40–0.45)</td>
</tr>
</tbody>
</table>

Reference province is Quebec. Adjusted for age, comorbidities, length of stay, treating physician, hospital type, and unique hospital identifier.
these patients, a restrictive policy for ARB use was associated with reduced use of ARBs.

Our results suggest that residing in a province with a restrictive drug policy may be associated with reductions in the use of evidence-based drug therapy for HF. Specifically, we found that a prior authorization policy reduced the use of ARBs, even among patients who were not receiving ACE-I and who would have likely been approved for ARB coverage. A number of possible explanations have been proposed for this observation, including physicians avoiding the hassle of preauthorization by simply not prescribing restricted drugs, or prescribing such drugs without preauthorization.25 Furthermore, our results also indicate that significantly limiting choice in BBs with multiple restrictive policies (such as in BC) was associated with important reductions in the use of this class of medications and with increased use of nonevidence based agents. This observation could be explained by a lack of alternatives among patients who did not tolerate first-line therapy (eg, metoprolol). Ensuring that alternate choices for each drug class are available without significant administrative hurdles may limit the effect of many of these restrictive policies while still containing costs, if the cost differential between the alternative medications is not substantial.

A major issue is whether the differences in drug use observed are truly related to effects of policy and not attributable to differences in patient, physician, or other province-level characteristics that may influence prescribing practices within provinces. To address this issue, we examined the use of drugs, such as loop diuretics and ACE-I, which were not restricted in any of the provinces. These drugs provided an estimate of the underlying variability in HF drug use between provinces without the effects of policy. In comparisons between ON and QC, we found adjusted ORs of 0.80 and 0.81 for ACE-I and loop diuretics (drugs not affected by policy in either province), respectively, suggesting that there are important regional differences in overall prescription patterns between these 2 provinces, even among nonrestricted drugs. Despite these regional differences, we found that in provinces with restrictive policies, restricted drugs (ARBs and BBs) were used significantly less frequently than nonrestricted drugs (loop diuretics and ACE-I) suggesting that policy restrictions are associated with markedly lower use of restricted HF medications over and above the existing regional differences in HF drug use.

Our findings of significant differences among unrestricted drugs also highlight the degree with which regional differences in care can affect prescriptions of medications and stress the importance of controlling for such regional differences when drawing inferences across regions. We found much larger regional differences in unrestricted drug use between BC and QC than between ON and QC, which limited our ability to find a significant association between policy and drug use in BC. Such regional differences have been documented for various aspects of care and have been attributed to regional level variables such as socioeconomic status or resource availability.26 Increased pharmaceutical marketing in regions with less restrictions could also explain

### Table 4. Baseline Characteristics of HF Patients Not Receiving ACE-I

<table>
<thead>
<tr>
<th>Age, y, mean±SD</th>
<th>QC</th>
<th>ON</th>
<th>BC</th>
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</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>44</td>
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<td>51</td>
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<td>Comorbidities, %</td>
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<td>Diabetes mellitus</td>
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<tr>
<td>Chronic renal failure</td>
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<tr>
<td>Cerebrovascular disease</td>
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<tr>
<td>Dementia</td>
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<table>
<thead>
<tr>
<th>Procedures, %</th>
<th>QC</th>
<th>ON</th>
<th>BC</th>
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<tr>
<td>Angiography</td>
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<tr>
<td>Admitting physician, %</td>
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<tr>
<td>General practitioner</td>
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<td>41</td>
<td>64</td>
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<td>Cardiologist</td>
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<td>Hospital type: teaching</td>
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</table>

IQR indicates interquartile range. P<0.001 for all covariates across provinces.
such regional disparities. Local preferences in care among patients and physicians may also contribute to such differences. Lastly, dissemination, uptake, and adherence to practice guidelines may differ by region.  

Our results on the effect of policy restrictions on medication use are consistent with previous studies that have shown that restrictive policies are associated with reduced drug use. Some of these studies have also shown that restrictive policies were associated with adverse clinical outcomes. A restrictive drug policy in California led to decreases in the use of ACE-I and statins among high-risk cardiac patients which led to increased hospitalizations. Similarly, cost-containment policies used in New Hampshire during the 1980s led to marked reductions of the use of essential drugs, particularly among the elderly, which led to increased use of health-care resources. Recently, a limited-use policy for clopidogrel was shown to reduce the use of this drug and was associated with worse outcomes. We have also recently reported that removal of a prior authorization policy on clopidogrel use in Canada was associated with improved access to clopidogrel and improved cardiovascular outcomes.  

Restrictive prescription plans clearly reduce the use of restricted medications and could lead to significant savings for payers of prescription drugs. Provincial governments in Canada formally evaluate the cost-effectiveness of new drugs before determining policy regarding reimbursement for medications on provincial formularies, but they often may vary their policy decisions in spite of having access to same body of scientific information. Because medical therapy often represents a highly cost-effective strategy for chronic disease management, economic benefits obtained from limiting access to medications through restrictive policies may be lost because of increased use of health-care resources and worse health outcomes over time. A recent study has shown that a strategy of providing full unrestricted drug coverage for postmyocardial infarction patients would reduce mortality while also being highly cost-effective. Alternatively, restrictive policies that decrease drug costs without affecting patient outcomes may represent an effective health care policy in light of limited health care budgets. It is important to note that we did not formally assess whether the drug policies we evaluated were associated with differences in outcomes or cost-effectiveness, and this should be the subject of future research. It should also be noted that Ontario has removed its restrictive policy on access to ARBs and β-blockers in heart failure patients since the time this study was conducted.  

Given that our study is a retrospective analysis of administrative data, a number of limitations apply. First, we created our HF cohort by merging 3 separate provincial administrative databases. It is possible that provincial differences in patient characteristics could limit comparisons between cohorts. All patients in our cohort were discharged from hospital with a new diagnosis of HF, which is known to be valid and accurate for these provinces. We also excluded patients with HF admissions within the 3 years before entry into the cohort to reduce differences in severity of illness. Despite our attempts to create comparable cohorts, patients from QC had a higher burden of comorbidities than patients from other provinces. Although we adjusted all parameter estimates for major covariates that may affect prescription use, residual confounding may still modify our estimates. We did not adjust for socioeconomic status or pharmaceutical marketing, as these variables were not available. In addition, physician identifiers were unavailable for all provinces, and therefore despite adjusting for clustering at the hospital level we could not account for physician level clustering in our data. We also did not consider differences in copayments between provinces. Nonetheless, we have previously reported that copayments among seniors between these provinces are similar and could not explain the differences in drug use observed.  

Second, we could not adjust for echocardiography or measures of ejection fraction. However, it is unlikely that the prevalence of systolic dysfunction was significantly different between these 3 provinces. It is however possible that differential use of echocardiography across provinces could have led to differences in documenting systolic dysfunction. However, we did adjust for treating physician and academic hospital status, which may act as surrogate markers for the utilization of echocardiography. Furthermore, we could not determine whether the lower rates of drug prescribing in ON and BC was a function of underuse of these drugs in patients with LV dysfunction or a reflection of greater rates of use of these drugs in patients with preserved systolic function, a group where most of these drugs have not been demonstrated to have outcome benefits. The former outcome would have been an undesirable impact of a restrictive drug policy, whereas the latter outcome might represent an undesirable outcome in the province with an unrestricted drug policy, because it would increase drug costs and exposure without necessarily improving patient outcomes.  

Third, our study evaluated the effect of restrictive policy only after such policies had been implemented. Such an “after-only” study design can lead to erroneous conclusions regarding the effect of policy. To strengthen our conclusions we included a control group which did not have a restrictive policy during the time of the study (QC). Furthermore, we used HF drug use not affected by a restrictive policy (ACE-I and loop diuretics) as a measure of the underlying variability in prescriptions between provinces. The use of nonrestricted drugs provided reasonable estimates of the regional differences in drug use between provinces. We found that regional differences in drug use between BC and QC remained large despite statistical adjustment, which limited our ability to evaluate the specific effects of the restrictive drug policy in BC. Despite a trend toward lower ORs for some restricted drugs in BC, we could not exclude the possibility that the differences in restricted drug use between BC and QC were attributable to other regional factors or chance.  

In summary, we have shown that residing in a province with a more restrictive prescription plan is associated with lower use of HF medications over and above the expected regional differences in HF drug use across provinces. Our results have important implications for public health and policy. Because of the rising costs of medications, public payers will continue to implement policies that attempt to
contain costs. However, because certain medications may be highly cost-effective for many chronic diseases such as HF, restrictive drug policies should be implemented with caution when they may affect such populations and should be evaluated for their impact on drug use, drug costs, and patient outcomes.

Acknowledgments

We thank Shun Fu Chen, Hassan Behlouli, and Jiming Fang for providing statistical support and Sonia Tremblay for helpful editorial comments during the preparation of this manuscript.

Sources of Funding

Dr Thanassoulis was supported by a research fellowship by the Fonds de Recherche en Santé du Québec and the Canadian Institute of Health Research. Drs Eisenberg and Pilote are supported by Senior Physician-Scientist Awards from the Fonds de Recherche en Santé du Québec and the Canadian Institute of Health Research. Dr Tu is supported by a Canada Research Chair in Senior Physician-Scientist Awards from the Fonds de Recherche en Santé du Québec and the Canadian Institute of Health Research Team Grant in Cardiovascular Outcomes Research. The Institute for Clinical Evaluative Sciences is supported by an operating grant from the Ontario Ministry of Health and Long-term Care. The results and conclusion are those of the authors and should not be attributed to any of the funding agencies.

Disclosures

None.

References


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Impact of Restrictive Prescription Plans on Heart Failure Medication Use
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Circ Cardiovasc Qual Outcomes. published online September 1, 2009;
Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-7705. Online ISSN: 1941-7713

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circoutcomes.ahajournals.org/content/early/2009/09/01/CIRCOUTCOMES.108.804351

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