The Impact of the Canadian Hypertension Education Program on Antihypertensive Prescribing Trends

Norman R.C. Campbell, Karen Tu, Rollin Brant, Minh Duong-Hua, Finlay A. McAlister; for the Canadian Hypertension Education Program Outcomes Research Task Force

Abstract—Although previous studies have shown that hypertension management has improved in Canada during the past decade, this study was designed to determine whether these changes were temporally related to initiation of the Canadian Hypertension Education Program in 1999. Antihypertensive prescription rates in Ontario were compared using time series analyses before and after 1999 in 2 Ontario cohorts: all hypertensives prescribed therapy (using the Intercontinental Medical Statistics CompuScript Database) and all elderly hypertensives without diabetes prescribed therapy (using linked administrative databases including the Ontario Drug Benefit Database). Between January 1998 and December 2003, ≈280 million prescriptions for antihypertensive agents were filled in Ontario, and total antihypertensive prescriptions increased by 58% annually; time series analyses confirmed that the prescribing rates for total antihypertensives, thiazide diuretics, β-blockers, and calcium channel blockers increased significantly after 1999, even after adjustment for the temporal trends in the pre-1999 data. In the 166 018 nondiabetic individuals over age 65 who were newly treated for hypertension in Ontario between July 1994 and March 2002, changes in prescription rates for total antihypertensive drugs, angiotensin-converting enzyme inhibitors, β blockers, and calcium channel blockers occurred in directions that were consistent with guideline recommendations and were statistically significantly related to the initiation of the Canadian Hypertension Education Program. The substantial changes in prescription rates for guideline-recommended antihypertensive drug classes in elderly Ontarians without diabetes and the general Ontario population seen in the past decade are temporally related to the initiation of the Canadian Hypertension Education Program. (Hypertension. 2006;47:22-28.)

Key Words: hypertension ■ drug therapy ■ prospective studies
rate of change in particular drug classes did not appear to be statistically different before/after the initiation of the CHEP process in 1999.8

There are 3 possible explanations for the discrepant findings from our 2 earlier studies: (1) CHEP had less impact in Ontario than the other Canadian provinces (because the IMS database included data from all of the Canadian provinces and our ODB database did not); (2) the impact of CHEP was different in younger hypertensive patients (who are included in the IMS database) than older hypertensive patients (who make up the ODB database sample); or (3) the impact of CHEP in older Ontarians with hypertension was obscured by our inclusion of hypertensive patients with diabetes in our ODB dataset analyses. To investigate these possibilities, we conducted the 2 studies described in this article to evaluate the following: (1) whether total antihypertensive prescriptions in Ontario (as collected in the IMS CompuScript database) changed after the implementation of CHEP, an analysis that addresses the first 2 possibilities above; and (2) whether antihypertensive prescribing in older Ontarians without diabetes (as collected in the ODB database) changed after CHEP, an analysis that addresses the last possibility for our previously discrepant findings.

Methods

Study Samples

All Treated Hypertensives in Ontario (Substudy 1)

For the first study, Ontario cardiovascular drug dispensing information was obtained from IMS Health-Canada. The IMS CompuScript database compiles monthly dispensing records from a representative sample of two thirds of all retail pharmacies. Based on standardized sampling weights, monthly Ontario estimates for the dispensing of individual drugs were calculated. Prescribing rates were “standardized” for population change using Statistics Canada intercensal annual population estimates for Ontario. Monthly population estimates were calculated based on the annual population estimates. The number of prescriptions dispensed for all of the antihypertensive agents between January 1998 and December 2003 (listing of drugs within each class available from first author on request) were examined. Combination tablets containing a diuretic with another antihypertensive drug were included in both the diuretic and the relevant nontiuretic class when we calculated class-specific rates but were counted only once for estimates of total antihypertensive prescribing. The CompuScript database does not include information on physician characteristics or patient-level data (eg, demographics, comorbidities, or concomitant medications dispensed).

IMS also links drug usage to indications for use, as reported by a representative random sample of Canadian office-based physicians. We used this survey data to examine changes in the proportion of antihypertensive drug classes being used for hypertension indications between 1998 and 2003.

All Treated Elderly Hypertensives in Ontario Without Diabetes (Substudy 2)

For the second study, the ODB prescription drugs database was used to identify all Ontario residents aged 66 years or older who had received a new (initial) prescription for an antihypertensive drug between July 1, 1994, and March 31, 2002. To ensure that our cohort was started on an antihypertensive agent for treatment of hypertension and not another indication, we cross-linked our cohort (using a unique encrypted number to preserve patient anonymity) with the Ontario Health Insurance Plan physician claims database, the Canadian Institute for Health Information hospitalization database, the Registered Persons Database, and the Ontario Diabetes database as described in our previous publication.6 We excluded those patients with diabetes or with any of the following: (1) Ontario Health Insurance Plan claims within 3 years; (2) Canadian Institute for Health Information claims within 4 years; or (3) prescriptions for marker medications in the ODB within 1 year for any of the following conditions: myocardial infarction or angina, heart failure, arrhythmias, renal disease (including nephropathy), liver disease (including esophageal varices), stroke or transient ischemic attack, hyperthyroidism, or migraines. Patients with a claim for an initial antihypertensive in the first 12 months of the study or during their first 12 months of ODB eligibility were excluded to ensure that our cohort consisted of newly treated patients; thus, all of the patients in the study were ≥66 years of age. Prescribing rates were standardized for population change using Statistics Canada intercensal annual population estimates for Ontario. Monthly population estimates were calculated based on the annual population estimates.

Determining the Impact of CHEP

Because the CHEP process began in 1999, we chose to examine prescribing practices before and after 1999 in both the IMS CompuScript analysis (of all treated hypertensives in Ontario) and the ODB database analysis (of all treated elderly Ontario hypertensives without diabetes). In January 1999, the CHEP guidelines recommended thiazide diuretics, β blockers, or ACE inhibitors for hypertensive patients under age 60 (long-acting calcium channel blockers were added to this list in January 2000) and recommended thiazide diuretics or long-acting calcium channel blockers for those > age 60 (ACE inhibitors were added to this list in January 2000).9,10 β-Blockers were specifically recommended against as first-line therapy in the elderly in 1999 (and subsequent iterations of the guidelines).

Data Analysis

Population-adjusted prescription rates are plotted on logarithmic scales in Figures 1 and 2. The smooth curves on the graphs, as well as the annualized prescription increases, were derived from the application of time-series models to logarithmically transformed prescription numbers. The curves in the graphs represent the predicted values from the model. The annualized prescription increases were calculated from linear combinations of the model parameters. All of the models included systematic components for periodic calendar variation plus a segmented “switching” linear regression (switching at January 1999). Residual errors were modeled as autoregressive moving average processes. Graphical inspection of residuals revealed no systematic departures from assumptions except for prescriptions for angiotensin receptor blockers. All of the computations were programmed in the R-project implementation of the S language. All of the reported P values are 2-sided, and we defined P<0.05 as statistically significant. To give the reader insights into clinical significance of the results, we chose to present 95% CIs around the estimates of 1999-related changes in prescribing patterns.

Results

All Treated Hypertensives in Ontario (Substudy 1)

Between January 1998 and December 2003, 280 million prescriptions for antihypertensive agents were filled in the study pharmacies. Antihypertensive prescriptions from all drug classes increased by 58% annually in Ontario between January 1998 and December 2003 (Figure 1), with class-specific annual increases of 416% for angiotensin receptor blockers (ARBs), 74% for thiazide diuretics, 70% for angiotensin-converting enzyme (ACE) inhibitors, 44% for β-blockers, and 25% for calcium channel blockers.

Time-series analyses confirmed that the rate of change in prescriptions for total antihypertensive drugs, thiazide diuretics,
Figure 1. Trends in prescriptions for antihypertensive drugs for Ontarians of all ages, January 1998 to December 2003 (substudy 1). Monthly data (○) as well as a line derived from nonparametric smoothing are shown for thiazide diuretics, β-blockers, ACE inhibitors, calcium channel blockers, angiotensin receptor blockers, and total antihypertensive prescriptions. The data were obtained from the IMS CompuScript database.
Overall, the rate of increase in ARB prescriptions declined after 1999; however, the statistical model did not fit the ARB data well because of the relatively small number of prescriptions and the rapidly changing rates. The use of combination drugs (2 drugs in 1 tablet) was declining before 1999 and increased after 1999 (rate change after CHEP, 13.5% increase per annum; 95% CI, 0.1% to 28.7%).

Overall, total antihypertensive prescriptions were growing at 2% per year before 1999 and increased 5-fold to 10% per year after 1999. The specific drug class prescription rates increased from 0.3-fold (angiotensin receptor blockers) to 6.5-fold (thiazide-type diuretics). Calcium channel blockers had a negative growth rate before 1999 and increased by >5% per year after 1999. There was little change in the proportion of antihypertensive drugs that were prescribed for nonblood pressure–lowering indications during this time (Table 2).


<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Percent of Prescriptions Reported To Be for the Treatment of Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1998</td>
</tr>
<tr>
<td>Diuretics*</td>
<td>58</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>49</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>75</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>64</td>
</tr>
</tbody>
</table>

Data from IMS Health Compuscript database.

*Includes all diuretic subclasses (ie, not just thiazides).

### Discussion

There have been large increases in antihypertensive prescription rates in Ontario since 1994, and in both of our study populations (all those prescribed antihypertensive drugs in Ontario and all elderly Ontarians without diabetes prescribed antihypertensive drugs), the rate of increase was significantly greater after initiation of CHEP than before. Moreover, in both of our analyses, the changes in specific drug classes mirrored the CHEP recommendations. Thus, our data confirm that the impact of CHEP was similar in Ontario to the overall Canadian population and that prescribing practices changed in both younger and older Ontarians with hypertension. Of the 3 possible explanations for the discrepant findings between our previous studies outlined in the introduction to this article, the analyses reported herein lead us to conclude that our previous inclusion of prescribing data for those patients with and without diabetes obscured the benefits of CHEP on nondiabetic hypertensive prescribing practices. Our findings are consistent with preliminary data from the Canadian Community Health Surveys 1994 to 2003 demonstrating a substantial increase in the proportion of self-reported hypertensive subjects who were prescribed antihypertensive drugs over time, with a statistically significant relationship to CHEP initiation in 1999.

It is worthy of emphasis that in all of the cases, shifts in prescribing rates for specific drug classes were consistent.
Figure 2. Trends in initial prescriptions for antihypertensive drugs in Ontarians >65 years of age without diabetes, July 1994 to March 2002 (substudy 2). Monthly data (•), as well as a line derived from nonparametric smoothing, are shown for thiazide diuretics, β-blockers, ACE inhibitors, calcium channel blockers, angiotensin receptor blockers, and total antihypertensive drugs. The data were obtained from the ODB database.
with CHEP recommendations. Although in most cases this meant a sharp increase in annualized prescriptions for drug classes that were already increasing pre-CHEP, in 2 cases these shifts were in directions opposite to the pre-1999 trends but consistent with the CHEP recommendations for/against those drug classes. For example, calcium channel blocker—prescribing rates were in decline pre-1999 but increased substantially and significantly in both elderly hypertensives without diabetes (substudy 2) and in hypertensives of all age groups (substudy 1) after they were endorsed by CHEP. On the other hand, prescribing rates for β-blockers in elderly hypertensives without cardiac disease, which had been increasing annually before the CHEP recommendation against first-line use of these drugs, exhibited a statistically significant decrease after the CHEP recommendation was disseminated (substudy 2). Although we readily acknowledge that many factors can be associated with increases in prescribing of specific drugs (including, but not restricted to, trial publications, pharmaceutical industry marketing, and clinical practice guidelines), it is worth noting that the marked increase in prescribing rates that we found for thiazide diuretics (in both populations we studied: elderly hypertensives without cardiac disease; however, we excluded patients with any of these comorbidities in our data from the National Public Health and Community Health Surveys in Canada 2000–2003 have shown that >80% of people with recognized hypertension are prescribed antihypertensive therapy,11 Whereas changes in underlying demographics (age, obesity, etc) could lead to changes in the prevalence of hypertension and thereby drive changes in total antihypertensive prescri-

TABLE 3. Percent Annual Change in Initial Prescription Rates for Antihypertensive Drugs in Elderly Ontarians Without Diabetes, Before and After the Introduction of the Canadian Hypertension Education Program in 1999 (Substudy 2)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Annualized % Change in Initial Prescription Rate 1994–1998</th>
<th>Annualized % Change in Initial Prescription Rate 1999–2002</th>
<th>Annual % Change in Prescribing Rate 1999–2002 vs July 1994–1998 (95% CI, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total antihypertensive drugs*</td>
<td>−0.6</td>
<td>5.6</td>
<td>6.2 (3.9 to 8.6)</td>
</tr>
<tr>
<td>Thiazide diuretics</td>
<td>0.6</td>
<td>2.1</td>
<td>1.4 (0.16 to 2.7)</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>0.8</td>
<td>−0.4</td>
<td>−1.2 (−2.1 to −0.3)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>−0.9</td>
<td>6.3</td>
<td>7.2 (5.3 to 9.2)</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>−2.0</td>
<td>1.3</td>
<td>3.4 (1.2 to 5.5)</td>
</tr>
<tr>
<td>Angiotensin receptor blockers</td>
<td>0.3</td>
<td>1.0</td>
<td>0.7 (0.5 to 0.9)</td>
</tr>
</tbody>
</table>

Data from the Ontario Drug Benefit database.
*Total antihypertensive drugs include diuretics, ACE inhibitors, angiotensin receptor blockers, β-blockers, and calcium channel blockers, as well as miscellaneous antihypertensive drugs.

Our findings contrast with the failure of other national hypertension guidelines to influence prescribing patterns (including earlier iterations of the Canadian guidelines before initiation of CHEP).12–16 We believe that the multifaceted implementation processes, which are an integral part of the CHEP guidelines (which incorporate local opinion leader–led small group workshops and individual academic detailing alongside traditional passive dissemination techniques, such as journal publications and mailed information packages), accounts for the effect of the CHEP recommendations, a view supported by the accumulated evidence proving the efficacy of these approaches.17–19 The robust evidence supporting the efficacy of antihypertensive therapy in large randomized, controlled clinical trials makes it likely that the increases in use of antihypertensive drugs, which we have observed, will have a positive effect on hypertension control rates and will lead to reductions in cardiovascular and cerebrovascular events.20

Because the 2 studies we report in this article are before–after observational designs, it is impossible to say for certain that CHEP was the causative factor driving the observed changes in prescribing practices. We acknowledge that pharmaceutical industry marketing undoubtedly has driven some of the increase in antihypertensive prescriptions over the past decade;21 however, by examining time trends before and after CHEP in time-series analyses, we were able to adjust for temporal trends. Furthermore, changes in the prescribing of β-blockers and thiazide diuretics corresponded to CHEP recommendations, and generic pharmaceutical companies in Canada largely produce these products (without marketing programs). We acknowledge that some antihypertensive therapies may be prescribed for indications other than hypertension (eg, ACE inhibitors may be prescribed for chronic kidney disease or atherosclerotic disease prevention independent of their blood pressure lowering effects); however, we excluded patients with any of these comorbidities in our second substudy (we could not do so in our first substudy, because the IMS CompuScript database does not include clinical data). Furthermore, there were no substantive changes in the indications reported by participating physicians for the use of antihypertensive drugs in the Canadian population during the time periods covered by this study. Indeed, some may point out that in using antihypertensive prescriptions to examine hypertension management, we will miss those patients who have hypertension but have not been prescribed therapy; however, data from the National Public Health and Community Health Surveys in Canada 2000–2003 have shown that >80% of people with recognized hypertension are prescribed antihypertensive therapy.11
tions, it is unlikely that a substantial change in the demographics of the Ontario population would have occurred in 1999 coincident with the CHEP initiation. Finally, it is possible that the plethora of major hypertension clinical trials published over the past decade20 drove some of the prescribing changes we observed. Although the impact of published clinical trials without reinforcing factors has been shown to be an inconsistent and minor influence on physician practice behaviors,19 we accept that the varying influence of trials and pharmaceutical industry advertising likely accounts for variations in prescribing rates for specific drugs.

Perspectives

We have demonstrated significant changes in the prescribing of antihypertensive drugs in Ontario that were consistent in time and direction with the initiation of the CHEP process in 1999. The magnitude of these changes was substantial: in Ontario the annualized increase in antihypertensive prescribing rates increased 5-fold (from 2% per annum to 10% per annum) after 1999. In some subgroups, the changes were even more profound; for example, in elderly Ontarians without diabetes, antihypertensive prescribing rates (which had been essentially flat from 1994 to 1998) increased by 6% per annum after 1999. The observational nature of our study precludes the making of definitive conclusions of a cause and effect relationship, and some may question our focus on a process of care outcome (antihypertensive prescribing) rather than clinical outcomes. A survey incorporating measurement of blood pressure in randomly sampled adults is soon to start in Canada, and additional studies examining the impact of the CHEP program on Canadian rates of death and hospitalization from stroke, heart failure, and myocardial infarction in hypertensive patients before and after CHEP are underway. Until such studies are completed, this study represents our best evidence supporting knowledge translation programs, such as CHEP and the National High Blood Pressure Education Program,22 for improving the management of hypertension and other atherosclerotic risk factors.

Acknowledgments

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References

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