PERSISTENCE WITH HYPERTENSION TREATMENT AMONG COMMUNITY-DWELLING BC SENIORS

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ABSTRACT

Background
Previous research has documented low levels of persistence with prescribed hypertension treatment in Canada. With growing recognition of the value of appropriate drug therapy, rates of persistence may be improving over time. The purpose of this study was to examine persistence with prescribed hypertension treatment among newly treated community-dwelling seniors in British Columbia.

Methods
BC PharmaCare data was used to determine the cohort of seniors who were newly-treated hypertensives over the period 1993 to 2000. Medical and hospital claims from the BCLHD were searched for diagnoses indicating the presence of essential hypertension and potentially confounding conditions. Rates of persistence with drug therapy were analysed, accounting for patient, age, sex, clinical complexity, the existence of potentially confounding conditions, and type of drug first prescribed.

Results
For the period 1993 to 2000, 82,824 seniors were identified as new users of hypertension drugs with diagnosed essential hypertension. Fifty-one percent of these newly-treated hypertensives filled a contiguous series of hypertension prescriptions for at least one full year. There was a slight improvement in the rate of persistence over time ($p<0.001$). Evidence of specific co-morbidities that potentially complicate essential hypertension increased the likelihood of persistence among first-time users ($p<0.001$), whereas greater overall clinical complexity decreased the likelihood of persistence ($p<0.001$). Persistence was highest amongst patients initiated on newer anti-hypertensive drug therapies.

Conclusions
Despite modest improvement, persistence with hypertension treatment among the elderly is very low. Further research into the reasons for non-persistence would be advanced through primary data collection, including survey-based research. New policies and practices are needed to encourage persistence with evidence-based therapies.

Keywords: Hypertension; insurance claim review; pharmaceutical use.

Essential hypertension is one of the most common chronic diseases, and is the leading primary diagnosis for patient visits to physicians' offices in Canada.[1]

For patients whose blood pressure cannot be successfully managed with diet and lifestyle modifications alone, pharmacological treatment can be a safe and effective means of reducing the risk of morbidity and mortality.[2-4] Clinical evidence concerning the efficacy of drugs to treat hypertension is based on controlled trials involving good levels of treatment persistence and adherence.

However, previous studies have documented a lack of adherence to prescribed treatments for hypertension.[5,6]

With growing recognition of the value of appropriate drug therapy, rates of persistence may be improving over time. The purpose of this study was to examine recent trends in the rate of persistence with prescribed hypertension treatment by newly treated community-dwelling seniors in British Columbia.

METHODS

Cohort definition

The study cohort was defined as community-dwelling seniors for whom administrative data revealed evidence of both first-time hypertension drug use and diagnosed essential hypertension.

BC PharmaCare data for 1991 to 2001, comprehensive for residents aged 65 and older, were used to identify first-time hypertension drug use. New users of hypertension drugs were defined as patients aged 66 or older for whom there were no prior PharmaCare claims for any hypertension drug, including angiotensin converting enzyme inhibitors (ACE-inhibitors), angiotensin-II receptor blockers (ARBs), beta-blockers, calcium channel blockers, thiazide diuretics, non-thiazide diuretics, and other anti-hypertensives (e.g. Rauwolfia and alpha-antagonists).

The study cohort was limited to newly treated hypertensives based on diagnostic information taken from the BC Medical Services Plan and Hospital Separations File of the BC Linked Health Database (BCLHD). The cohort was limited to patients for whom at least one ICD-9 diagnosis of essential hypertension could be found in administrative data spanning two years prior to and one year following the first purchase of a hypertension drug. Hypertension diagnoses following drug purchases were included because such diagnoses only appear after the initiation of drug treatment for nearly one-third of otherwise uncomplicated patients.

ICD-9 diagnostic codes for the two years before first hypertension drug purchase were also searched for indications of potentially confounding conditions. Chosen for their possible influence on drug choice and treatment regimen, and identified using 'Expanded Diagnostic Clusters'[7], the potentially confounding conditions included acute myocardial infarction, aneurysm, angina, congestive heart failure, cardiac arrhythmia, ischemic heart disease, cardiovascular valve disorders, gout, migraine headache, diabetes mellitus, and chronic renal failure. Although the research dataset spanned 1991 to 2001, the study cohort was limited to patients first treated between 1993 and 2000 because of data needed to define measures of co-morbidity and persistence.

Persistence Measure

Based on methods used elsewhere, [6, 8] the measure of "persistence" with therapy required that a patient fill a contiguous series of prescriptions for hypertension drugs for a period of at least one year following her or his first hypertension prescription purchase.

A discontinuation was assumed to have occurred if the dispensed supply of drug ran out before a subsequent prescription was filled. A 'prescribed days supply' measure was calculated based on the number of units of pills dispensed in a given prescription divided by the average dosing for the dispensed product across all prescriptions for that product under PharmaCare.

To bias methods against over-reporting discontinuation, the minimum supply of drug per prescription was assumed to be 120 days, which is the amount equal to the PharmaCare program's maximum plus a twenty percent margin. Switches between different types of hypertension drug were not considered a discontinuation in therapy.

Statistical Analysis

Summary statistics describing rates of persistence were computed. Multivariate logistic regression analysis was conducted to determine influences on the probability that a patient would persist with treatment. Independent variables for the multivariate analysis included patient age, sex, and year of first prescription.

As a measure of overall clinical complexity, the regression included a count of the number of different types of prescription drugs purchased within one year prior to each patient's first hypertension drug purchase.[9] Binary variables indicating prior diagnosis of potentially confounding conditions were included along with variables identifying the type of drug prescribed at the initiation of therapy. Wald chi-squared tests

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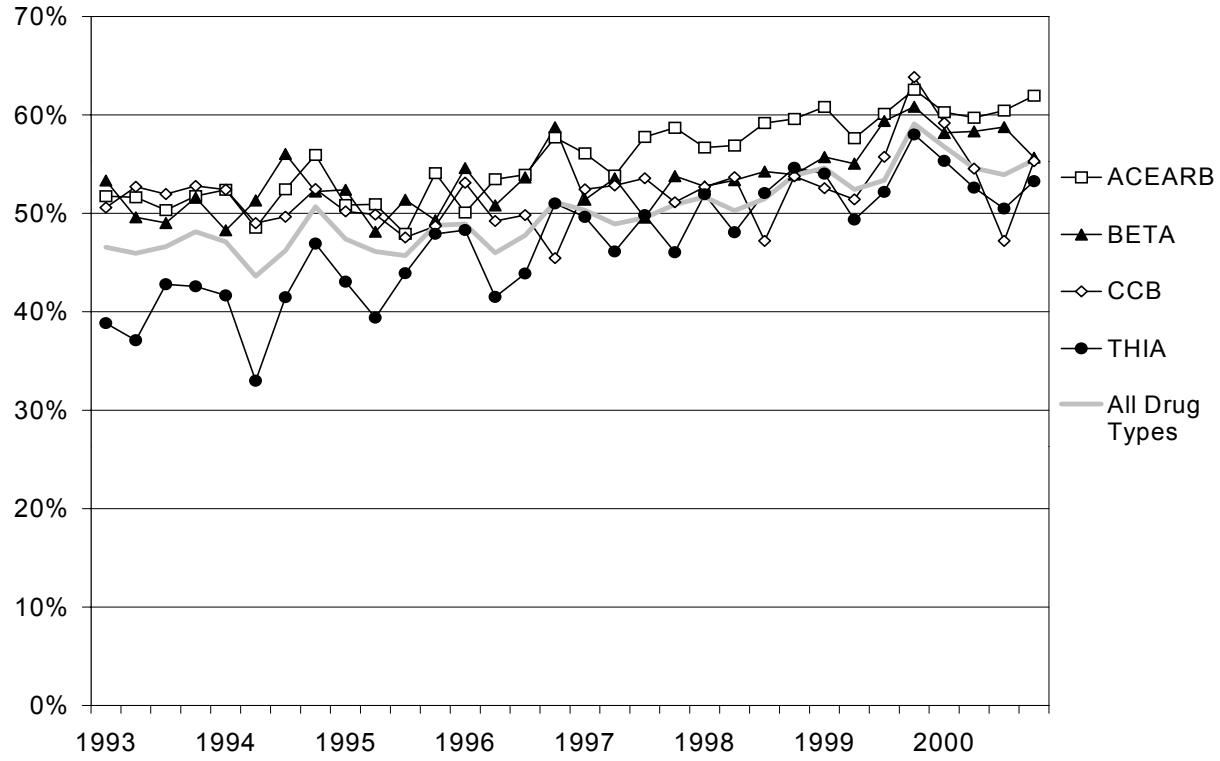
were calculated to determine statistical significance.

RESULTS

For the study period, a total of 82,824 community dwelling seniors were identified as new users of hypertension drugs with diagnosed essential hypertension. Fifty-one percent (41,921) of these newly treated hypertensives were persistent with therapy for one full year following their first hypertension drug use.

FIGURE 1 Rate of persistence with therapy for at lest one year by newly treated hypertensives in each quarter, 1993 to 2000



ACEARB = Angiotensin converting enzyme inhibitor or Angiotensin II receptor blocker
BETA = Beta-Blockers
CCB = Calcium channel blockers
THIA = Thiazide Diuretics

Figure 1 illustrates the share of newly treated hypertensives in each quarter-year that persisted with therapy for at least one year following their first purchase of a prescribed hypertension medicine. The figure depicts trends in persistence for each of the leading categories of anti-hypertensives (ACE-Inhibitors or ARBs, calcium channel blockers, beta-blockers, and thiazide diuretics).

Beginning in 1996, persistence with treatment increased for all leading drug classes. Persistence with thiazides appeared to increase most notably over the period of study, rising from well below overall average to a rate roughly equal to overall average. Overall, the rate of persistence among newly treated patients increased from an average of 47 percent in the period spanning 1993 through 1996 up to an average of 55 percent in 2000.

TABLE 1 Persistence with therapy for at least one among all newly treated senior hypertensives, by drug type, 1993 to 2000.

	Patients Newly Treated	Persistent for 1+ years	%
All Drug Types	82,824	41,921	51%
Angiotensin converting enzyme inhibitor or Angiotensin II receptor blocker	23,861	13,452	56%
Beta-Blockers	14,842	8,017	54%
Calcium channel blockers	11,914	6,175	52%
Thiazide Diuretics	15,278	7,467	49%
Thiazide + Others	8,433	3,642	43%
Other Diuretics	7,502	2,823	38%
Other Hypertension Drugs	994	345	35%

Table 1 summarizes the total number of patients newly treated over the period of study by type of hypertension drug. As has been found elsewhere, the rate of persistence with therapy was highest among patients whose first purchase of a hypertension drug was for an ACE-inhibitor or ARB.[5]

Just over half (56%) of those patients started on an ACE-inhibitor or ARB persisted with therapy for at least one year. Persistence with therapy was slightly lower among patients whose first purchase was for beta-blockers, calcium-channel blockers, or thiazide diuretics. persistence was lowest among patients whose first purchase was for combined therapies of thiazide diuretics with other hypertension drugs, for non-thiazide diuretics, or for other anti-hypertensive drugs. Regression analysis revealed that aneurysm, gout, and renal disease were not significantly associated with the probability of persisting with treatment.

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TABLE 2 Odds ratios from logistic regression: probability of persisting with therapy for at least one year*

	Point Estimate	95% Wald Confidence Limits	
Year of first Rx	1.056	1.049	1.062
Age at first Rx	0.996	0.994	0.998
Sex (1=Female)	1.199	1.166	1.234
Number of Different Drugs Prior	0.950	0.945	0.955
Acute Myocardial Infarction	1.549	1.433	1.675
Congestive Heart Failure	1.303	1.217	1.395
Cardiovascular Valve Disorders	1.165	1.092	1.242
Angina	1.081	1.036	1.128
Ischemic Heart Disease, Other	1.060	1.012	1.110
Diabetes	1.055	1.017	1.094
Arrhythmia	1.053	1.005	1.104
Migraine	0.852	0.758	0.958
Angiotensin converting enzyme inhibitor or Angiotensin II receptor blocker	1.384	1.328	1.443
Calcium Channel Blockers	1.210	1.151	1.271
Beta-Blocker	1.169	1.115	1.226
Thiazide + Other	0.816	0.773	0.861
Diuretic (other)	0.641	0.603	0.680
Other Hypertension Drugs	0.614	0.536	0.703

Note: All estimates statistically significant from 1.00 at p=0.01

*The reference case is a 66-year-old male with no co-morbidities who first purchased a thiazide diuretic.

Table 2 lists odds ratios calculated from the multivariate regression excluding those potentially confounding co-morbidities. In the regression model, all coefficient estimates were statistically significant at a size of 0.05. There was a statistically significant time-trend toward increased rates of persistence ($p<0.001$). Older patients were less likely to be persistent with therapy than younger patients, and women were approximately twenty percent more likely than men to persist with treatment.

The number of different prescription drugs received in the year prior to hypertension treatment, a measure of the patient's overall

clinical complexity, was significantly associated with decreasing probability of persistence. In contrast, a higher probability of persistence was estimated for patients with evidence of one or more of several specific conditions that could potentially complicate essential hypertension, including, acute myocardial infarction, congestive heart failure, cardiovascular valve disorders, angina, ischemic heart disease, diabetes, or arrhythmia. Patients with a history of migraine headaches were less likely to persist with hypertension treatment.

Drugs chosen to initiate therapy appear to have a significant impact on the probability of persistence for at least one year. Patients whose first purchased prescription was an ACE-inhibitor or ARB, a beta-blocker, or a calcium-channel blocker were significantly more likely to persist with treatment than those whose initial purchase was a thiazide product. Patients whose first purchase was for thiazide diuretics in combination with other products, for non-thiazide diuretics, or for other anti-hypertensive drugs were less likely to persist with treatment than those whose initial purchase was a thiazide product.

CONCLUSIONS

Despite gradual improvements, persistence with drug treatment among newly treated BC seniors with hypertension was very low in the late 1990s.Even with generous assumptions, which would bias toward over-reporting persistence, only half of newly treated senior hypertensives persisted with drug treatment for at least one year.

The findings of this study also indicate that elderly patients whose first drug purchase is for newer products, such as ACE-inhibitors and ARBs, have higher rates of persistence with therapy than those started on other drugs. Though the absolute value of differences is modest, they are nevertheless statistically significant and deserve attention for their possible impact on health outcomes. The findings of this study, as with others based on similar methods, must be interpreted with some caution, for it is limited by the constraints of administrative data. For example, algorithms for determining persistence using administrative data may not capture strategies such as pill-splitting that may be used to extend the length of prescriptions.

Furthermore, administrative data do not contain information about samples given to patients. This may bias the results toward over-reporting persistence for patients whose first purchase is for a sampled product, discontinuation after the use of a professional sample but before filling any prescriptions would not be accounted for in administrative data. Given the difference in vintages of products, such a bias may explain the comparatively high rate of persistence among patients whose first purchased drug was one of the relatively new treatments. Alternatively, manufacturers' promotions to prescribers and patients about the benefits of newer products may encourage greater persistence. Such promotional activity does not occur for off-patent, 'generic' products.[10] The effects of such dynamics cannot be estimated with administrative data alone.

The findings of this study are consistent with other Canadian research on the treatment of hypertension and hyperlipidaemia.[6, 8, 11] Accumulated evidence in this area clearly points to a need for research on non-persistent drug use. It is possible that pharmaceuticals are being appropriately used for temporary management of conditions such as hypertension until diet and lifestyle are modified sufficiently, or that patients engage in forms of dosage modification not captured by administrative data. It is also possible that patients lose interest in treating sub-clinical risk factors that are not 'felt' in the same way as the acute illness.

Research into the potential reasons for apparent non-persistence could be advanced through primary data collection. Survey-based audits of patient behaviour and/or chart-audits of recorded blood pressures and disease management practices could yield greater insight into the causes and potential consequences of non-persistence. Ideally, such insights would inform new policies and practices to encourage persistence with evidence-based therapies.

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REFERENCES

1. IMS. 2002 Canadian Pharmaceutical Industry Review: Diagnoses and Therapies. Montreal http://www.imshealthcanada.com/htmen/pdf/IMSR02_T31-32.pdf [Accessed Jan 28 2004]: IMS Health, Canada; 2003.
2. Ogilvie RI, Burgess ED, Cusson JR, Feldman RD, Leiter LA, Myers MG. Report of the Canadian Hypertension Society Consensus Conference: Part 3. Pharmacologic treatment of essential hypertension. CMAJ 1993; 149(5):575-84.
3. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jr., et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289(19):2560-72.
4. ICES. Management of Hypertension: Diagnosis, Evaluation, When to Treat and Non-Pharmacological Therapy. Toronto: Institute for Clinical Evaluative Sciences http://www.ices.on.ca/docs/fb1420.htm [Accessed 9/25/98]; 1998.
5. Caro JJ, Speckman JL, Salas M, Raggio G, Jackson JD. Effect of initial drug choice on persistence with antihypertensive therapy: the importance of actual practice data. CMAJ 1999; 160(1):41-46.
6. Caro JJ, Salas M, Speckman JL, Raggio G, Jackson JD. Persistence with treatment for hypertension in actual practice. CMAJ 1999; 160(1):31-37.
7. Johns Hopkins University. ACG Software Documentation & Users Manual. Baltimore, MD: Johns Hopkins University; 2001.
8. Jackevicius CA, Mamdani M, Tu JV. Adherence With Statin Therapy in Elderly Patients With and Without Acute Coronary Syndromes. JAMA 2002; 288(4):462-467.
9. Metge C, Kozyrskyj AL, Roos N. Pharmaceuticals: focusing on appropriate utilization. Winnipeg: Manitoba Centre for Health Policy; 2003.
10. Morgan SG, Mintzes B, Barer M. The economics of direct-to-consumer advertising of prescription-only drugs: prescribed to improve consumer welfare? Journal of Health Services Research and Policy 2003; 8(4):237.
11. HSURC. Adherence to Cholesterol-Lowering Drugs in Saskatchewan. Saskatoon: Health Services Utilization and Research Commission; 1997 September.