Persistence with treatment for hypertension in actual practice

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Abstract

Background: Despite the existence of efficacious medications, many patients in actual practice remain with uncontrolled hypertension. Randomized clinical trials, cannot address this issue well given their highly restricted environment. This paper examines persistence with antihypertensive therapy among patients in actual practice.

Methods: Cohort study of patients who received a diagnosis of hypertension and were treated between 1989 and 1994 identified through the Saskatchewan Health databases. Patients with concurrent diagnoses likely to affect initial treatment choice were excluded. The resulting population of 79 591 subjects was grouped into those with established hypertension (52 227 [66%]) and those with newly diagnosed hypertension (27 364 [34%]). The initial antihypertensive prescription, subsequent changes in treatment and persistence with antihypertensive therapy were analysed.

Results: Persistence with antihypertensive therapy decreased in the first 6 months after treatment was started and continued to decline over the next 4 years. Of the patients with newly diagnosed hypertension, only 78% persisted with therapy at the end of 1 year, as compared with 97% of the patients with established hypertension ($p < 0.001$). Among those with newly diagnosed hypertension, older patients were more likely than younger ones to persist, and women were more likely than men to persist ($p < 0.001$).

Interpretation: This analysis of actual practice data indicates that barriers to persistence occur early in the therapeutic course and that achieving successful therapy when treatment is started is important to maintaining long-term persistence.

Résumé

Contexte : Même s'il existe des médicaments efficaces, dans la réalité, beaucoup de patients continuent de vivre avec une hypertension non contrôlée. À cause de leur environnement très restreint, les études cliniques randomisées ne peuvent pas bien répondre à ce problème. On examine dans ce document dans quelle mesure les patients persévèrent et suivent une thérapie aux antihypertenseurs dans la réalité.

Méthodes : Étude de cohortes de patients chez lesquels on a diagnostiqué une hypertension et qui ont été traités entre 1989 et 1994, repérés dans les bases de données du ministère de la Santé de la Saskatchewan. On a exclu les patients chez lesquels d'autres diagnostics simultanés pouvaient jouer sur le choix du traitement initial. On a regroupé les 79 591 sujets en groupes dont l'hypertension était déjà établie (52 227 [66 %]) et chez lesquels on venait de diagnostiquer une hypertension (27 364 [34 %]). On a analysé l'antihypertenseur prescrit initialement, les modifications subséquentes du traitement et la persévérance avec laquelle les sujets ont suivi la thérapie aux antihypertenseurs.

Résultats : La persévérance avec laquelle les sujets ont suivi le traitement aux antihypertenseurs a fléchi au cours des six premiers mois qui ont suivi le début du traitement et continué à fléchir au cours des quatre années suivantes. Parmi les patients chez lesquels on venait de diagnostiquer une hypertension, 78 % seulement suivaient toujours le traitement à la fin de la première année, comparative-

Evidence

Études

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ment à 97 % des patients qui avaient une hypertension établie ($p < 0,001$). Parmi les sujets chez lesquels on venait de diagnostiquer une hypertension, les patients plus âgés étaient plus susceptibles de persévérer que les plus jeunes, et les femmes l'étaient plus que les hommes ($p < 0,001$).

Interprétation : Cette analyse de données tirées de la pratique réelle indique que des obstacles à la persévérance font leur apparition au début du traitement et que la réussite au début du traitement joue un rôle important dans la persévérance à long terme.

Hypertension is the single most common and most important risk factor for cardiovascular disease.[1,2] Continuous drug treatment has been found to decrease the rates of both death and sickness associated with hypertension.[3–7] Numerous medications are currently available for hypertension treatment, all with similar efficacy in lowering blood pressure and comparable rates of side effects in clinical trials.[8] Despite this, several surveys have shown that many patients have diagnosed, but uncontrolled, hypertension.[9–11] Lack of adherence to treatment has been postulated as a potentially important reason for this finding.[12–14]

The consequences of lack of adherence to treatment cannot be easily understood from clinical trial data because the tight control imposed in trials may artificially increase compliance.[15] Although some studies of adherence in actual practice have been done, they have generally suffered from at least one limitation: populations that mix patients who have established hypertension with those who have newly diagnosed hypertension, short follow-up, small sample or failure to exclude patients with coexisting illnesses that may affect treatment decisions.[16–21] One recent study was not hampered by these problems, but it focused on an elderly population insured through Medicare in the United States.[22] Another study considered only 2 classes of hypertensive medications, calcium-channel blockers and angiotensin-converting-enzyme (ACE) inhibitors.[23]

Our study was designed to examine persistence with antihypertensive treatment among patients in actual practice. In this paper we describe the source population and its context, the databases used and the methods implemented to deal with the problems encountered in working with databases of this type. We report on persistence with antihypertensive therapy and its relation to age, sex and previous use of health care resources.

Methods

Source population and environment

We conducted the study using the health care databases managed by Saskatchewan Health.[24] These extensive, electronically linked health data[25] pertain to residents covered by provincial health insurance. Apart from Native Canadians, who are not included in the outpatient drug database, less than 1% of the remaining residents are not covered. Approximately 76% of families are standard (deductible and copayment) beneficiaries; the remainder qualify for increased drug plan benefits based on factors including income, disability and emergency assistance.

There were 3 deductible rates for the prescription drug plan during the period of this study.[26] For families, the deductible increased from $125 annually before May 1992 to $190 semiannually until March 1993. For single seniors it went from $50 annually to $50 semiannually, and for senior families from $75 annually to $75 semiannually. After March 1993 the deductible for all groups increased to $850 semiannually. For seniors in special support programs the deductible may be reduced. Copayment for standard beneficiaries also changed: from 20% before March 1991 to 25% until May 1992 and then to 35% with a $375 maximum until March 1993; after this time the copayment was 10%. In addition, as of March 1991, coverage for brand-name drugs was limited to the price of the least expensive drug within an interchangeable group, and in 1991 a limit of 3 refills within 45 days was implemented.

Cohort definition

Patients who received at least 1 antihypertensive prescription between Jan. 1, 1989, and Dec. 31, 1994, were identified. The date of the first prescription was defined as the index date. Men and women were eligible if, at the index date, they were 40 years or older and had a recorded diagnosis of essential hypertension (codes 401, 401.1 and 401.9 in the International Classification of Diseases, ninth revision [ICD-9][27]) but not hepatic, renal or other cardiovascular disease. Subjects who were pregnant at the index date were excluded.

By examining the data for the first 10 months of 1989, we classified patients as having established or newly diagnosed hypertension. If there were prior prescriptions, a patient was assigned to the established hypertension group, with a start date of Nov. 1, 1989. Otherwise the patient was considered to have newly diagnosed hypertension, the start date being the index date. For both groups, the date of emigration from the province, the date of death or Dec. 31, 1994, whichever came first, was the end date. Individual observation time was calculated as the number of days between the start and end dates.

Data collection

For all eligible subjects the database was searched for all

dispensings of an antihypertensive drug during the study period. The resulting 3 878 100 records identified the antihypertensive medication by its generic name and American Hospital Formulary Service classification, the dispensing date, quantity, strength and drug form, unit drug price and no-substitution indicator. Although information on the actual prescription (e.g., posology) was not included, for convenience these will be termed "prescriptions" in this paper.

Similar data were also obtained on 4 842 865 prescriptions for drugs other than antihypertensive agents received by the patients, and information was collected on all doctor visits (5 766 292 records) and hospital admissions (157 748 records).

Apart from eligibility data, we also obtained information on the date of diagnosis of hypertension and the date that health benefits started. Information on blood pressure was not available.

Regimen reconstruction

The actual antihypertensive regimen was not specified. For example, two sequential records for different antihypertensive agents may mean that the second drug was added or may mean a switch. To reconstruct the regimens, we developed a computer program that used information on dispensing date, amount dispensed, type of drug and tablet scoring combined with the estimated minimally effective dosage and maximum daily dosage. The logic is illustrated in Fig. 1 for a simplified case. For this case, from the 14 records showing dispensings of 3 agents, the computer program deduces 4 regimens: A alone, then A in combination with B, then B alone, and, finally, C alone.

If the computer algorithm could not settle on a regimen or if the result appeared highly unusual (e.g., regular frequent cycles of noncompliance), the crude data were examined directly by 2 internists (J.J.C. and M.S.). A graphic sequence of prescriptions and hospital admissions for the patient was displayed along a time axis to allow for visual inspection of the relation of various dates. The regimen reconstruction rules were refined after these time series were examined. The final computed regimens were verified by visual inspection on a sample of 100 test cases and on all outliers.

Once the regimens were determined, it was possible to consider the therapeutic course in terms of any changes, such as additions, switches and deletions, in the pattern of regimens as well as gaps in medication availability. The lower panel of Fig. 1 shows the therapeutic course for a hypothetical patient.

To determine whether a patient persisted with antihypertensive therapy, we examined the last recorded prescription in relation to the end date. Patients who did not have a medication to take at that time were considered nonpersistent. For those whose antihypertensive regimen consisted of more than 1 drug, this possibility was considered only if they ran out of all antihypertensive medications. By considering the maximum dosage, the analysis allowed for the accumulation of medication for later use. For example, this could happen if a patient received 2 prescriptions of the same drug on the same day (perhaps to take on vacation). As drugs dispensed in a hospital are not recorded in the database, we used hospitalization records to determine whether admission explained the nonpersistence.

The longer the discontinuation, the more likely it is to be permanent. Thus, we examined the influence of varying grace periods on the results. The reasons for nonpersistence, including whether it followed the physician's advice, could not be determined. Also, for patients deemed persistent, we could not be sure that they actually took the medication as prescribed.

Statistical analysis

We performed all statistical analyses using SAS-Windows (version 6.12, SAS Institute, Inc., Cary, NC). We used χ^2 analysis, Student's *t*-test and analysis of variance where appropriate. Since patients began treatment at different times during the study period and, thus, were followed for differing lengths of time, we used Kaplan–Meier failure time analyses[28] to estimate the cumulative persistence rates, with patients be-

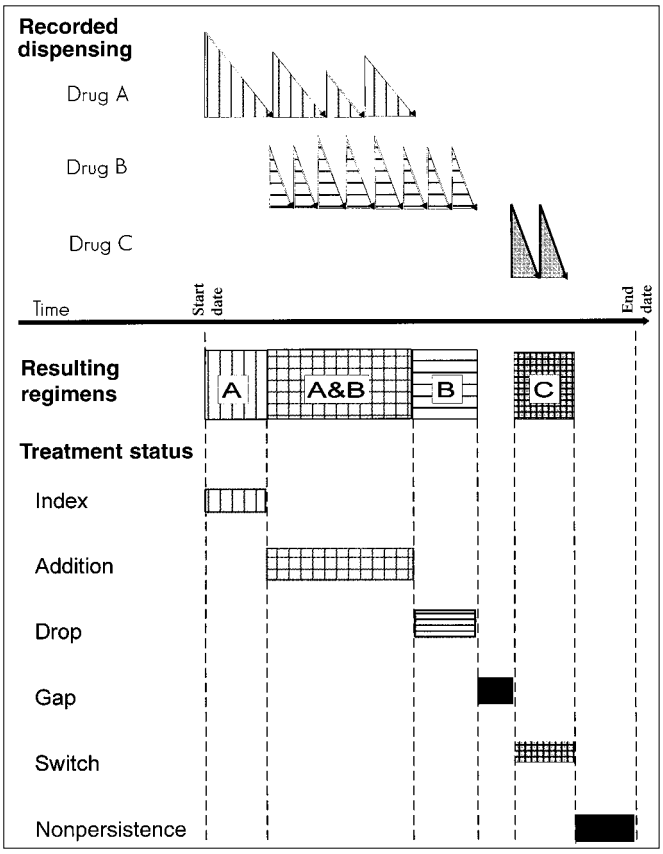


Fig. 1: Drug regimen reconstruction and definition of changes illustrated for a hypothetical patient. Top panel shows dispensing of drugs A, B and C. The height of each vertical line reflects the amount of drug dispensed, and the diagonal arrow shows its predicted consumption. The regimens deduced from these records are depicted in the centre bar. The bottom panel shows the changes in regimen and their time course. There is a gap in compliance between the third and fourth regimens. The final period of noncompliance lasts until the end of observation and therefore is defined as nonpersistence.

ing censored at the end of their observation time if they still persisted with therapy. The log-rank test was used for comparisons. In analyses in which only persistence over a defined period was considered, we used logistic regression to examine the effects of several determinants simultaneously. One important factor that may affect the likelihood of persistence is health status. We used 3 measures of health status: the number of physician visits, the number of hospital admissions and the number of prescriptions for drugs other than antihypertensive agents in the year before the index date or, for patients with newly diagnosed hypertension, the year before starting therapy. In addition to these factors, we also considered age and sex in the analyses. All continuous factors were modelled with the use of indicator variables.

Results

Study population

We obtained data for 79 602 subjects, of whom 11 were excluded because their diagnosis was malignant hypertension (ICD-9 code 401.0). Of the remaining 79 591 patients, nearly two-thirds (62%) were women, and a similar proportion were 60 years of age or more (median age 65 years). A total of 27 364 patients (34%) had newly diagnosed hypertension. The mean observation period for the latter patients was 1015 (standard deviation 544) days (range 1 to 1887 days), a total of 76 055 person-years of observation. The mean observation period for the patients with established hypertension was 1742 (standard deviation 365) days (range 1 to 1887 days), a total of 249 121 person-years. In analyses of persistence, only the 74 181 patients followed for at least 1 year were included. Of these, 22 875 had newly diagnosed disease.

Patients with established hypertension tended to be older than those with newly diagnosed hypertension (median age 66 years v. 63 years) ($p < 0.001$) and to be female (65% v. 57%) ($p = 0.001$). There were 7164 deaths, most (80%) among patients with established hypertension. In terms of prior health status, more patients in the established group had 12 or more physician visits (Fig. 2). In both groups, advanced age (60 years or more) and female sex were associated with worse prior health status in terms of a higher rate of resource use ($p < 0.05$).

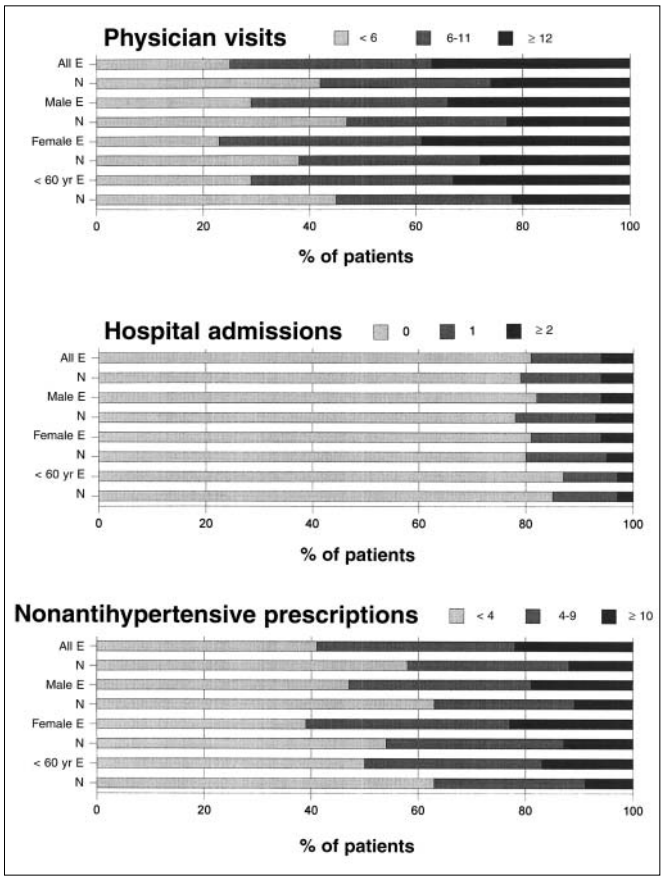


Fig. 2: Number of physician visits, hospital admissions and prescriptions for medications other than antihypertensive agents among 27 364 patients with newly diagnosed hypertension (N) in the year before beginning antihypertensive therapy, and among 52 227 patients with established hypertension (E) in the first year of observation.

Index regimens

During the study period the Saskatchewan formulary consisted of 56 different antihypertensive medications: 12 diuretics, 9 β-blockers, 6 calcium-channel blockers, 7 ACE inhibitors, 10 combination medications and 13 other agents. Among the patients with newly diagnosed disease, diuretics were the most frequent index regimen (38%), and ACE inhibitors were the next most frequent (28%). A total of 13% of the patients began with a calcium-channel blocker, and 11% with a β-blocker. Other medications accounted for the remaining 10%. Triamterene and hydrochlorothiazide combined in one tablet was the single most common index regimen (17%).

Among the patients with established hypertension, diuretics were also the most common index regimen (34%). Regimens consisting of 2 or more drugs were the second most common (27%). ACE inhibitors, β-blockers and single-tablet combinations each accounted for about 10% of the index regimens, and calcium-channel blockers and other drugs accounted for the remainder.

Persistence

The patients with established hypertension generally persisted with therapy throughout the study period: 97% were persistent at 1 year and 82% at 4.5 years. Persistence was much lower among those with newly diagnosed disease (78% and 46% respectively) ($p < 0.001$) (Fig. 3).

Among the patients with newly diagnosed hypertension, women were more persistent than men, but the gap closed with time: at 1 year, 80% of women and 77% of men were persistent, but at 4.5 years the corresponding values were 47% and 46% ($p < 0.001$). There was a similar difference between older and younger patients: 79% v. 77% at 1 year, and 47% v. 45% at 4.5 years ($p < 0.001$).

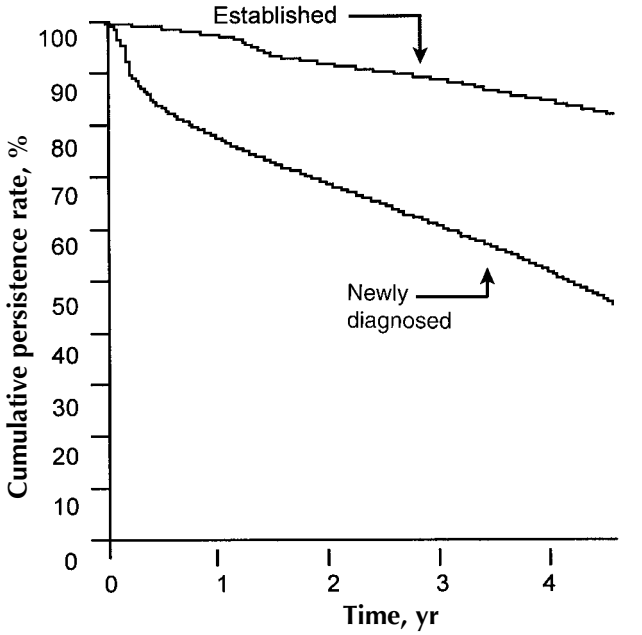
Logistic regression analyses of persistence through the first year confirmed that patients with established hypertension were much more likely to persist with therapy than those with newly diagnosed disease (odds more than 10-fold higher) (Table 1). The other factors exerted much less influence. Although both age and sex remained significant, the effect was relatively small. As might be expected, patients who visited the doctor frequently or had many other prescriptions in the prior year were more likely to persist with therapy, even if they had newly diagnosed hypertension.

In these models, nonpersistence is considered a permanent condition. It is possible, however, that some patients resume filling prescriptions for antihypertensive therapy after the observation period. The shorter the period of nonpersistence, the more likely it may have been only a temporary gap between prescriptions. The mean duration of nonpersistence was substantial, however: 846 (median 571) days for the patients with newly diagnosed hypertension and 1538 (median 1885) days for those with established hypertension. In both groups, less than 1% had a period of nonpersistence of less than 14 days (0.5% for the newly diagnosed group and 0.2% for the established group). Removing the data for these patients from the analyses did not alter the significance or direction of the results.

Interpretation

We found persistence with antihypertensive pharmacotherapy in actual practice to be remarkably poor within 5 years after treatment was started. As expected, patients with newly diagnosed hypertension were much less likely to persist with therapy. Among the patients with newly diagnosed disease, women and older patients were more persistent initially.

For this report we analysed information on prescriptions for over 79 000 patients. There are advantages to using this prescription database. It provides a wealth of information about a population that is relatively stable, as emigration and immigration are monitored to ensure



Established				
Not persistent	1 372	2 900	1 567	2 124
n	50 149	46 244	43 573	40 171
Newly diagnosed				
Not persistent	5 869	1 985	1 431	1 182
n	18 460	13 616	9 359	4 877

Fig. 3: Cumulative rate of persistence with antihypertensive therapy for the 2 groups. The table shows the number of patients who stopped persisting each year and the number of patients observed at least that long. Patients who persisted with therapy to the end of their observation time were censored on the last day of their follow-up.

Table 1: Odds ratio of persistence with antihypertensive drug therapy through the first year for patients in Saskatchewan, 1989–1994

	Group; odds ratio (and 95% confidence interval)	
Characteristic	All patients *n = 74 181*	Patients with newly diagnosed hypertension *n = 22 875*
Established hypertension	10.73 (10.01–11.49)	–
Female sex	1.16 (1.10–1.23)	1.10 (1.03–1.18)
Age ≥ 60 yr	1.11 (1.05–1.18)	1.08 (1.01–1.16)
Hospital admission	0.75 (0.70–0.81)	0.80 (0.74–0.87)
> 5 physician visits in previous yr	1.59 (1.48–1.71)	1.93 (1.78–2.11)
> 3 other prescriptions in previous year	1.29 (1.22–1.37)	1.30 (1.21–1.39)

complete health plan coverage.[25] Extensive validation of the database has been reported.[29–31]

There are limitations though. Some important information is not available in this administrative database. The demographic information is limited to age and sex. No individual patient information was available on factors such as income, ethnic background or risk factors for heart disease. Whether these modify persistence with drug therapy is unclear.

Most important, although the ICD-9 diagnosis of hypertension was included in the database, blood pressure measurements, at diagnosis or during follow-up, were not available. Therefore, we were unable to relate persistence with therapy to blood pressure control. It is widely recognized, however, that discontinuation of antihypertensive therapy often leads to uncontrolled hypertension,[32] and, thus, these patients are at greater risk for a cardiovascular event.

Because information about deaths and migrations was included in the analysis, it is unlikely that nonpersistence can be explained by a failure to account for patients who have left the province. It is possible, however, that some patients did not persist with therapy for quite good reasons. If hypertension resolves gradually, the physician may stop treatment soon after starting it. This may occur because of biologic variability, measurement error or "white-coat hypertension." To reduce this possibility, it is currently recommended that physicians obtain several blood pressure measurements on at least 2 occasions.[33,34] It is not possible to know how regularly this was done in the study population. Nevertheless, it seems unlikely that this early resolution would entirely explain the significant numbers of patients who stopped drug therapy.

The patterns that we observed are unlikely to be unique to the population of Saskatchewan. Residents of this province are similar in incidence of heart disease to other populations in North America and Europe.[25,35] Moreover, there is no reason to believe that the practice patterns are unusual.

Although there are limitations to the data in our analyses, the results indicate a degree of nonpersistence too large to attribute solely to these limitations. The desired goal of keeping hypertensive patients on treatment is not being achieved adequately in actual practice. Our analyses emphasize the importance of maximizing the likelihood of successful early treatment of hypertension and thus increasing the proportion of patients taking medication over the long term. Until this is achieved, we will continue to fail in meeting this important public health goal.

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References

1. Kannel WB. Blood pressure as a cardiovascular risk factor. *JAMA* 1996;275: 1571-6.
2. Levy D, Larson MG, Vasan RS, Kannel W, Kalon K. The progression from hypertension to congestive heart failure. *JAMA* 1996;275:1557-62.
3. Moser M. Historical perspective on the management of hypertension. *Am J Med* 1986;80:1-11.
4. Gueyffier P, Froment A, Gouton M. New meta-analysis of treatment trials of hypertension: improving the estimate of benefit. *J Hum Hypertens* 1996;10:1-8.
5. Neaton JD, Grimm RH, Prineas RJ, Stamler J, Grandits GA, Elmer PJ, et al. Treatment of Mild Hypertension Study. Final results. Treatment of Mild Hypertension Study Research Group. *JAMA* 1993;270:713-24.
6. SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension: final results of the Systolic Hypertension in the Elderly Program (SHEP). *JAMA* 1991;265:3255-64.
7. Medical Research Council Working Party. MRC trial of treatment of mild hypertension: principal results. *BMJ* 1985;291:97-104.
8. Drugs for hypertension. *Med Lett Drugs Ther* 1995;37:45-50.
9. Stockwell DH, Madhavan S, Cohen H, Gibson G, Alderman MH. The determinants of hypertension awareness, treatment and control in an insured population. *Am J Public Health* 1994;84:1768-74.
10. Mancia G, Sega R, Milesi C, Cesana G, Zanchetti A. Blood pressure control in the hypertensive population. *Lancet* 1997;349:454-7.
11. Joffres MR, Hamet P, Rabkin SW, Gelskey D, Hogan K, Fodor G. Prevalence, control and awareness of high blood pressure among Canadian adults. Canadian Heart Health Surveys Research Group. *CMAJ* 1992;146:1997-2005.
12. Hershey JC, Morton BG, Davis JB, Reichgott MJ. Patient compliance with antihypertensive medication. *Am J Public Health* 1980;70:1081-9.
13. Lücher TF, Vetter H, Siegenthaler W, Vetter W. Compliance in hypertension: facts and concepts. *J Hypertens* 1985;3:3-9.
14. Bittar N. Maintaining long-term control of blood pressure: the role of improved compliance. *Clin Cardiol* 1995;18:312- 6.
15. Pablos-Méndez A, Barr G, Shea S. Run-in periods in randomized trials. *JAMA* 1998;279:222-5.
16. Jones JK, Gorkin L, Lian JF, Staffa JA, Fletcher AP. Discontinuation of and changes in treatment after start of new courses of antihypertensive drugs: a study of a United Kingdom population. *BMJ* 1995;311:293-5.
17. Hamilton RA, Briceland LL. Use of prescription-refill records to assess patient compliance. *Am J Hosp Pharm* 1992;49:1691-6.
18. Elliott WJ. Discontinuation rates for ACE inhibitors and calcium antagonists in a tertiary hypertension clinic [abstract]. *Am J Hypertens* 1993;6:94A.
19. Shea S, Misra D, Ehrlich MG, Field L, Francis CK. Correlates of nonadherence to hypertension treatment in an inner-city minority population. *Am J Public Health* 1992;82:1607-12.
20. Sharkness CM, Snow DA. The patient's view of hypertension and compliance. *Am J Prev Med* 1992;8:141-6.
21. Cooper JK, Love DW, Raffoul PR. Intentional prescription nonadherence (noncompliance) by the elderly. *J Am Geriatr Soc* 1982;30:329-33.
22. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Levin R, Avorn J. The effects of initial drug choice and comorbidity on antihypertensive therapy compliance: results from a population-based study in the elderly. *Am J Hypertens* 1997;10(7 pt 1):697-704.
23. Okano GL, Rascati KL, Wilson JP, Remond DD, Grabenstein JD, Brixner DI. Patterns of antihypertensive use among patients in the US Department of Defense database initially prescribed an angiotensin-converting enzyme inhibitor or calcium channel blocker. *Clin Ther* 1997;19:1433-45.
24. McAlister FA, Teo KK, Lewanczuk RZ, Wells G, Montague TJ. Contemporary practice patterns in the management of newly diagnosed hypertension. *CMAJ* 1997;157:23-30.

25. Malcolm E, Downey W, Stand LM, McNutt M, West R. Saskatchewan Health's linkable data bases and pharmacoepidemiology. *Post Mark Surveillance* 1993;6:175-264.
26. *Annual statistical report 1994–1995*. Regina: Saskatchewan Health Prescription Drug Services Branch. Government of Saskatchewan; 1996. p. 3.
27. Brouch KL, Bowers CR, Aaron WS, editors. *St Anthony's ICD9CM code book*. Reston (VA): St Anthony Publishing; 1994.
28. Kalbfleisch JD, Prentice RL. *The statistical analysis of failure time data*. New York: John Wiley & Sons; 1980. p. 10-9.
29. Tennis P, Bombardier C, Malcolm E, Downey W. Validity of rheumatoid arthritis diagnoses listed in the Saskatchewan Hospital Separations Database. *J Clin Epidemiol* 1993;46:675-83.
30. Rawson NS, Malcolm E. Validity of the recording of ischaemic heart disease and chronic obstructive pulmonary disease in the Saskatchewan health care datafiles. *Stat Med* 1995;14:2627-43.
31. Rawson NSB, Malcolm E, D'Arcy C. Reliability of the recording of schizophrenia and depressive disorder in the Saskatchewan health care datafiles. *Soc Psychiatry Psychiatr Epidemiol* 1997;32:191-9.
32. Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure. The sixth report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC-VI). *Arch Intern Med* 1997;157:2413-46.
33. Reeves RA. Does this patient have hypertension? How to measure blood pressure. *JAMA* 1995;273:1211-8.
34. Pierdomenico SD, Mezzetti A, Lapenna D, Guglielmi MD, Mancini M, Salvatore L, et al. "White-coat" hypertension in patients with newly diagnosed hypertension: evaluation of prevalence by ambulatory monitoring and impact on cost of health care. *Eur Heart J* 1995;16:692-7.
35. American Heart Association. *1998 heart and stroke statistical update*. Dallas: The Association; 1997. p. 7.

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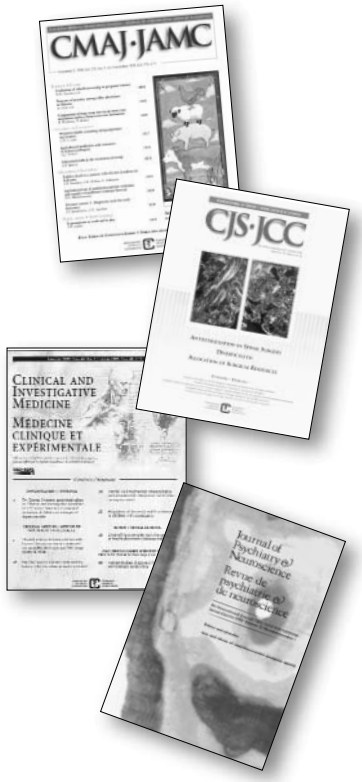

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