Treating hypertension

Are the right drugs given to the right patients?

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ABSTRACT

OBJECTIVE To evaluate whether physicians are prescribing antihypertensive drugs appropriately and according to the recommendations of the Canadian Hypertension Society.

DESIGN Retrospective cohort study.

SETTING Family medicine teaching clinic in Montreal.

PARTICIPANTS A cohort of 183 patients followed between 1993 and 1995. Of 350 patients registered at the clinic, 167 were excluded because diagnosis of hypertension was not supported by chart review, their charts contained insufficient information, they were pregnant or younger than 18 years, or they had secondary hypertension and complex medical conditions.

MAIN OUTCOME MEASURES The dependent variable was the antihypertensive medication. Independent variables were age and sex of patients, duration of hypertension, total number of visits and number of visits for hypertension, number of physicians consulted at the clinic, associated medical conditions, diagnosis of target organ damage, blood pressure readings, and associated medications.

RESULTS Diuretics were prescribed most frequently (45.9%). Angiotensin-converting enzyme (ACE) inhibitors ranked second (28.4%), followed by calcium channel blockers (26.2%) and β-blockers (18.0%). Age, sex, duration of hypertension, and blood pressure readings were not associated with medications. Prescription of β -blockers was strongly associated with previous myocardial infarction, but not with diagnosis of angina pectoris. Patients with contraindications to \(\beta\)-blockers were less likely to receive them and more likely to receive calcium channel blockers. Only 32% of diabetic patients received ACE inhibitors.

CONCLUSION Results suggest that some prescriptions for antihypertensive medications are inappropriate, but that physicians are following some of the Canadian Hypertension Society's recommendations. A better understanding of physicians' prescribing behaviours could help target continuing education interventions to improve prescribing for hypertension.

RÉSUMÉ

OBJECTIF Évaluer dans quelle mesure les médecins prescrivent correctement les antihypertenseurs et respectent les recommandations de la Société canadienne d'hypertension.

DEVIS Étude rétrospective d'une cohorte.

MILIEU Clinique d'enseignement de la médecine familiale située à Montréal.

PARTICIPANTS Cohorte de 183 patients suivis entre 1993 et 1995. Des 350 patients inscrits à la clinique, 167 furent exclus pour les raisons suivantes : diagnostic d'hypertension non supporté par une vérification des dossiers, documentation insuffisante dans les dossiers, grossesse, patient de moins de 18 ans, hypertension secondaire et conditions médicales complexes.

PRINCIPALES MESURES DES RÉSULTATS La variable dépendante fut la médication antihypertensive. Les variables indépendantes furent : âge et sexe des patients, durée de l'hypertension, nombre total des visites et nombre des visites pour hypertension, nombre de médecins consultés à la clinique, conditions médicales associées, diagnostic d'atteinte d'un organe cible, lectures de la tension artérielle et médications concomitantes.

RÉSULTATS Par ordre de fréquence, les médicaments les plus souvent prescrits furent : diurétiques (45,9 %), inhibiteurs de l'enzyme de conversion de l'angiotensine (28,4 %), antagonistes calciques (26,2 %) et bêta-bloquants (18,0 %). On n'a pas établi d'association entre ces médications et l'âge, le sexe, la durée de l'hypertension et les lectures de la tension artérielle. Par contre, on a établi une forte association entre les prescriptions de bêta-bloquants et les antécédents d'infarctus du myocarde ; cette association n'a toutefois pas été établie avec l'angine de poitrine. Les patients chez qui les bêta-bloquants étaient contre-indiqués furent moins susceptibles de les recevoir mais plus susceptibles de recevoir des antagonistes calciques. Seulement 32 % des diabétiques ont reçu des inhibiteurs de l'ECA.

CONCLUSION Les résultats indiquent qu'un certain nombre d'ordonnances d'antihypertenseurs sont inadéquates mais que les médecins respectent quelques unes des recommandations de la Société canadienne d'hypertension. Une meilleure compréhension des habitudes de prescription des médecins permettrait de mieux cibler les interventions de formation médicale continue et d'améliorer les ordonnances touchant le traitement médical de l'hypertension.

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ypertension is among the most frequently encountered health problems in primary care. The many clinical practice guidelines for hypertension have been remark-

ably consistent in recommending initial therapeutic choices: diuretics and β -blockers have been recommended as first-choice therapy by expert panels around the world.¹⁴

Some studies, however, suggest that physicians, particularly in North America, do not apply these guidelines.⁵⁻¹⁵ Diuretics are the most frequently prescribed drugs, but angiotensin-converting enzyme (ACE) inhibitors and calcium channel blockers, which are more expensive, are prescribed more often than is recommended as first-choice therapy.^{6-8,10-13} For example, Psaty et al,⁸ in a study of prescribing trends, observed that newly treated hypertensive patients were about half as likely as previously treated patients to receive diuretics or β-blockers and about twice as likely to receive calcium channel blockers or ACE inhibitors.

Although hypertension treatment guidelines are remarkably consistent, they are also remarkably complex. First-choice drugs might be contraindicated because of associated medical conditions. Because hypertension often is associated with myriad other chronic diseases, it is possible that only a few patients actually are able to take diuretics or β -blockers, making it difficult to ascertain how widely clinical practice strays from the guidelines.

Few studies have reported on factors associated with the choice of antihypertensive medication. Many of those studies are surveys of reported prescribing practices^{6,7,14-18} rather than descriptive studies based on chart review or database analysis.^{8,9,11-13,19} Some authors have reported that younger patients tend to receive ACE inhibitors more frequently than older ones, but this has not been observed consistently.^{6,9} In a survey conducted in Sweden, female and older physicians chose diuretics as first-line therapy more often than younger male physicians did.⁷ Some authors suggest that general practitioners choose less expensive treatment strategies more frequently than specialists, an observation that does not take

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into consideration the difference in case severity between the two groups of physicians. ^{15,20} We found only two studies where comorbidity was ascertained. One was conducted in a health management organization¹³; the other was based on a study of a community of residents older than 65 years. ⁹ In neither study was comorbidity associated with choice of therapy. ^{9,13}

Our study aims to evaluate the appropriateness of prescribing antihypertensive drugs according to the latest recommendations of the Canadian Hypertension Society, 1,21,22 in a cohort of patients followed for at least 2 years in a family medicine unit in Montreal.

METHOD

Setting

The study took place in a teaching unit affiliated with the Family Medicine Program at the University of Montreal. The clinic, which opened in 1988, serviced a mostly French-speaking population and was located in a poor socioeconomic area of Montreal. (At that time, the Quebec provincial government paid the full cost of prescription drugs for disadvantaged and elderly people.) The unit had 13 regular staff physicians, nine of whom practised full time at the teaching unit, and 13 family medicine residents on rotation for 2 years. In 1994, the clinic entered all its patient records into a computerized register. Two fourthyear medical students (functioning as clinical clerks at the externship level) effected the transfer under the supervision of one of the authors (M-D.B.). We reviewed records of the previous 2 years' visits to establish an active problem list, which we captured in the computerized database.

Study population

To be eligible, patients registered as having hypertension had to be regular patients of the clinic (not walk-in patients), who had consulted at least once a year between 1993 and 1995 and who had been treated for hypertension by a family physician at the clinic rather than by a specialist at the hospital. Charts were excluded if diagnosis of hypertension was not supported by chart review; if charts contained insufficient information; if patients were pregnant or younger than 18 years; or if patients were suffering from secondary hypertension and presenting with complex medical conditions, such as severe cardiac failure, atrial fibrillation with anticoagulant therapy, and metastatic cancer. Of the 350 patients registered since 1988, 183 met the eligibility criteria. Reasons for exclusion appear in **Table 1**.

Table 1. Reasons for exclusion from the study: 167 of 350 patients were excluded.

REASON FOR EXCLUSION	N	(%)
Only one or no consultation between 1993 and 1995	122	(73.1)
Not followed at the clinic for hypertension	20	(12.0)
Diagnosis not supported by chart review	11	(6.6)
Multiple complex medical conditions	10	(6.0)
Insufficient information in the chart	3	(1.8)
Secondary high blood pressure (renal artery stenosis)	1	(0.6)
TOTAL	167	

Variables

Variables were extracted from the charts by the same person (L.D.), who had been trained by the two other authors (M-D.B. and D.C.). Interobserver agreement was not measured formally, but periodic checks of the data abstraction process were conducted during the study. As previously mentioned, to be included in the analysis, charts had to contain information on patients' problems, blood pressure readings, and medications. Only three charts were excluded, which illustrates the high quality of the clinic's charts.

All visits were reviewed to ascertain treatment modifications and occurrence of new health problems. The dependent variable was the antihypertensive medication. Mean blood pressure reading was considered an outcome variable and readings at each visit as independent variables that could explain treatment modifications. Other independent variables were age and sex of patients, duration of hypertension, total number of visits and number of visits for hypertension during the study period, number of physicians consulted at the clinic, number of consultations with specialists, associated medical conditions, diagnosis of target organ damage, and associated medications.

Analysis

 χ^2 and Student's *t* tests were used for nominal and continuous variables, respectively. Logistic regression analysis was performed to evaluate factors associated with the probability of receiving each major

class of medication (diuretics, β-blockers, calcium channel blockers, and ACE inhibitors). Control variables were medical conditions considered indications or contraindications, age and sex of patients, presence of target organ damage, duration of hypertension, and systolic and diastolic blood pressure. The SPSS 6.0 software for Windows was used.

RESULTS

Patient characteristics are presented in **Table 2**. Mean age of subjects was 67.2 years (range 25 to 93 years; median 68 years). Mean duration of hypertension was 4.2 years (range 2 to 9 years; median 3.9 years). Most patients were followed by just one physician (mean number of physicians 1.69): 160 (87.4%) by staff physicians and 23 (12.6%) by family medicine residents. Patients averaged 6.2 visits for hypertension during the 2-year study period. One third of patients had no associated medical conditions; slightly less than a third had signs of target organ damage. Mean blood pressure readings remained stable during the study period: 151/85 mm Hg ± 18/10 at the beginning and 147/84 mm Hg ± 18/8 at the end.

Of the 183 patients, 15 (8.2%) received no medication, 103 (56.3%) received one medication, and 65 (35.5%) received combined therapy (seven received three medications). We observed modifications to the therapeutic regimen for only 11 patients (6%). Enalapril (eg, Vasotec) was the most frequently prescribed drug (15% of all prescriptions), followed by the combination of hydrochlorothiazide and triamterene, Diazide and others (11.5%). Regrouped as classes of medications, however, diuretics ranked first (45.9%), followed by ACE inhibitors (28.4%), calcium channel blockers (26.2%), and β-blockers (18.0%). **Figure 1** shows the distribution of antihypertensive medications for patients on monotherapy and combined therapy. The distribution of medications is comparable for both groups. Angiotensin-converting enzyme inhibitors and calcium channel blockers were preferred to β -blockers as monotherapy.

Only 20% of patients with coronary artery disease were receiving β -blockers; 32% of diabetics were receiving ACE inhibitors. **Table 3** shows the results of logistic regression analyses. Age, sex, duration of hypertension, and blood pressure readings were not associated with any class of medication and do not appear in the table. Prescription of β -blockers was strongly associated with antecedents of myocardial infarction, but not with diagnosis of angina pectoris.

As expected, patients with contraindications to β -blockers were less likely to receive them and more likely to receive calcium channel blockers. Patients with target organ damage were less likely to receive thiazide diuretics, but more likely to receive ACE inhibitors (P = 0.09).

DISCUSSION

Our results agree with others in the literature in suggesting that clinical practice guidelines on pharmacologic treatment of hypertension are not being implemented consistently. In our patients, although diuretics were the most frequently prescribed class of medication, enalapril was the most commonly prescribed drug and ACE inhibitors ranked second. Many diabetics, however, were not prescribed ACE inhibitors. β -Blockers were preferred only for patients who had already had myocardial infarctions and not for most patients with coronary disease who had no other contraindications.

Strengths

Our study has two strengths: it is based on observations of actual prescribing practices rather than on reported practices, and it has documented thoroughly patients' clinical conditions. To our knowledge, only two other studies have considered comorbidity as an explaining factor, and, in those studies, the authors did not identify any relationship between associated conditions and prescribing practices. ^{9,13} They do not report clearly, however, which clinical factors were considered, which hampers comparison with our findings.

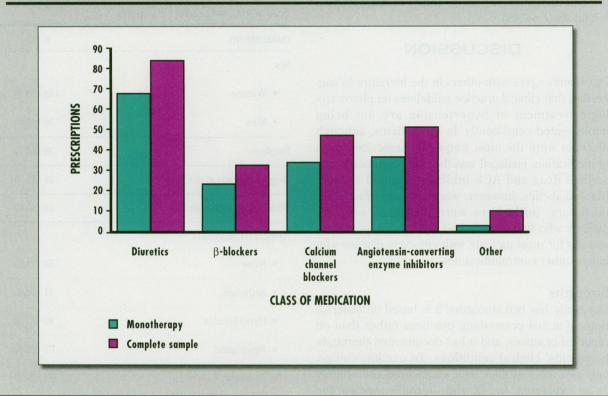
Limitations

This study has limitations. Only one clinical setting was studied and the number of patients was small. A retrospective approach to data collection has shortcomings. Were all hypertensive patients identified? How valid are medical records as a source of information on patient care? In 1994, researchers estimated that about 15% of hypertensive patients were not identified correctly by their doctors.⁵ Perhaps as many as 20% to 80% of patients who visit physicians do not have their blood pressure measured.²³ The objective of our study, however, was not to estimate the prevalence of hypertension in our practice. There is no reason to suspect that underidentification of hypertension is associated with a systematic bias in estimating the prescribing choices of physicians. Underidentification could lead to underestimating the

Table 2. Demographic and medical characteristics of the 183 patients: They made a mean of 10.9 visits overall and a mean of 6.2 (\pm 5.6) visits for hypertension. The women's mean age was 68.4 years, men's was 62.7 years

CHARACTERISTICS	N (%)	
Sex		
• Women	144 (79.1)	
• Men	39 (21.3)	
Smokers	38 (20.8)	
Diagnosis made at the clinic	28 (15.3)	
With target organ damage	56 (30.6)	
Associated diagnoses		
• None	58 (31.7)	
Arthrosis	41 (22.4)	
Hyperlipemia	40 (21.8)	
Psychiatric	39 (21.3)	
• Diabetes	37 (20.2)	
Chronic obstructive pulmonary disease	34 (18.6)	
Cardiac disease	29 (15.8)	
Intracardiac thrombus or acute cardiovascular disease	16 (8.7)	
Medications		
Benzodiazepine	48 (26.2)	
Nonsteroidal anti-inflammatory drug	46 (25.1)	
Acetaminophen	26 (14.2)	
Hypoglycemic	18 (9.8)	
Bronchodilator	19 (10.4)	
Antidepressant	20 (10.9)	
Antihistamine	18 (9.8)	
Hormonotherapy (women)	16 (8.7)	
Insulin	3 (1.6)	

Figure 1. Distribution of prescriptions according to medication class for patients receiving monotherapy (n = 103) and for the complete sample of patients receiving pharmacotherapy (n = 168)



number of patients not treated, if this phenomenon is associated preferentially with mild hypertension.

Some studies on the validity of medical records as sources of information allow us to be confident in the data obtained from the charts. In a classic study, Romm and Putnam²⁴ observed that information in medical records corroborated transcripts of actual encounters at 92% for the chief complaint, 71% for description of current illness, and 73% for diagnosis. To further validate our observations, we excluded all charts for which data were either insufficient (three) or did not support a diagnosis of hypertension (11). We suggest that there is no systematic association between potentially missing information and the type of pharmacologic treatment prescribed. Finally, the fact that the study clinic is a teaching setting can be considered a limitation also. The physicians, however, appear to share the prescribing practices of most North American physicians. 9,11,13-15 The proportion of patients receiving monotherapy in our study (about 50%) is comparable to that observed in larger cohorts.11,13

Our patient population consisted mostly of elderly women. It is possible that we did not have a sufficient number of young and middle-aged men to reveal specific prescribing tendencies for them. In a Canadian study, Vanasse et al¹¹ observed that diuretics and β-blockers tended to be prescribed more frequently to patients older than 60 years. Other studies did not report any association between age and sex of patients and prescribing practices.^{6,9,13} New research results can modify treatment guidelines; our observations and all previous results were reported before the STONE²⁵ study, which suggested that long-acting nifedipine (eg, Adalat) might help reduce complications from cerebrovascular disease.²⁵

Clinical practice guidelines

There seems to be a problem with implementing clinical practice guidelines on the pharmacologic treatment of hypertension. The right drugs are not necessarily given to the right patients. Our results suggest, however, that some recommendations are being followed. The contraindications to β -blockers

Table 3. Factors associated with prescription of antihypertensive medications: Results of logistic regression

MEDICATION	ODDS RATIO (95% CONFIDENCE INTERVALS)							
	ANGINA	MYOCARDIAL INFARCTION	DIABETES	TARGET ORGAN DISEASE	CONTRAINDICATIONS TO β-BLOCKERS	CONTRAINDICATIONS TO THIAZIDE		
Thiazide	1.83 (0.43-7.78)	1.33 (0.17-9.90)	*	0.42† (0.18-0.96)	0.89 (0.34-2.35)	0.39 (0.11-1.40)		
β-blockers	1.57 (0.35-7.08)	8.75 [†] (1.30-58.78)	‡	0.78 (0.36-1.69)	0.15† (0.08-0.56)			
Calcium channel blockers	1.79 (0.58-5.51)	0.44 (0.09-2.10)	1.29 (0.94-1.78)	1.37 (0.86-2.19)	2.81 [†] (1.26-6.26)			
ACE inhibitors§	0.37 (0.10-1.330)	0.55 (0.11-2.72)	0.88 (0.45-1.72)	1.66 (0.90-3.02)				

^{*}Included in contraindications to thiazide.

appear to be well known, as is their indication for patients who have had myocardial infarctions. Still. we should be concerned that β-blockers were not the preferred choice for patients with coronary disease and that ACE inhibitors, although prescribed for most patients, were not prescribed for most diabetics, for whom they are the first choice. It is unlikely that socioeconomic factors can be blamed because, in Quebec, at the time of the study, elderly people and those on social welfare. who constituted a large part of our cohort, did not pay for drugs.

Interestingly, the trend in favour of calcium channel blockers and ACE inhibitors is not as strong in Europe, 7,14,15,18 Australia, or New Zealand. 6,16 Aggressive marketing of these new classes of medication (relying strongly on the bad publicity about the side effects of the first β-blockers) and lack of marketing of β-blockers probably explain the trend. Still, recent studies of second-generation \(\beta \)-blockers do not support the bad press that these medications receive.²⁶⁻²⁸ The pharmaceutical industry appears to

Key points

Family physicians prescribed diuretics most frequently, followed by ACE inhibitors, and then β-blockers. Enalapril (eg, Vasotec) was the most commonly prescribed medication, although only one third of diabetics received it. β-Blockers appear to be underused.

be more effective at disseminating its messages than guideline developers are.

We cannot generalize our findings, but they suggest that some guideline recommendations are implemented well. Part of the discrepancy between practice and clinical guidelines might be due to the guidelines' complexity. Emphasizing all recommendations equally could have hampered communication of a clear message. Too many recommendations might be as bad as too few. A better understanding of the problem could help focus the messages on the most questionable prescribing behaviours. We need studies such as this one on a larger scale and in various settings if we are to plan effective continuing medical education to improve physicians' prescribing practices for hypertension.

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References

1. Ogilvie RI, Burgess ED, Cusson JR, Feldman RD, Leiter LA, Myers MG. Report of the Canadian Hypertension Society Consensus Conference: 3. Pharmacologic treatment of essential hypertension. Can Med Assoc J 1993;149:575-84.

 $^{^{\}dagger}P < 0.05$.

[‡]Included in contraindications to β-blockers.

 $^{^{\$}}$ Chronic obstructive pulmonary disease OR = 0.96 (CI 0.49-1.90), cardiac failure OR = 0.53 (CI 0.07-4.32).

P = 0.09.

RESEARCH

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- Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. Fifth report. Arch Intern Med 1993:153:154-83.
- 3. Server P, Beevers G, Bulpitt C, Lever A, Ramsay L, Reid J, et al. Management guidelines in essential hypertension: report of the second working party of the British Hypertension Society. *BMJ* 1993;306:983-7.
- Subcommittee of the WHO/ISH Mild Hypertension Liaison Committee. Summary of the 1993 World Health Organisation–International Society of Hypertension guidelines for the management of mild hypertension. *BMJ* 1993;307:1541-6.
- Furberg CD, Berglund G, Manolio TA, Psaty BM.
 Overtreatment and undertreatment of hypertension. *J Intern Med* 1994;235:387-97.
- 6. Steven ID, Wilson DH, Wakefield MA, Beilby J, Coffey GA, Esterman AJ, et al. South Australian hypertension survey. General practitioner experiences with drug treatment. *Med J Aust* 1992;156:641-4.
- 7. Stromme HK, Botten G. Factors related to the choice of antihypertensive and hypnotic drug treatment in old patients. *Scand J Prim Health Care* 1992;10:301-5.
- Psaty BM, Koepsell TD, Yanez ND, Smith NL, Manolio TA, Heckbert SR, et al. Temporal patterns of antihypertensive medication use among older adults, 1989 through 1992.
 An effect of the major clinical trials on clinical practice? JAMA 1995;273:1436-8.
- 9. Psaty BM, Savage PJ, Tell GS, Polak JF, Hirsch CH, Gardin JM, et al. Temporal patterns of antihypertensive medication use among elderly patients. The cardiovascular health study. *JAMA* 1993;270:1837-41.
- 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 stipulation. BMJ 1995;311:293-5.
- 11. Vanasse P, Laplante P, Delisle E, Grant A, Bernier R. Monothérapie et hypertension non compliquée: données du régistre provincial FAMUS. *Hypertension Can* 1995; Juillet: 3-7.
- 12. Quraeshi S. Tendances en matière de prescription d'antihypertenseurs : dans l'ensemble, des gains importants pour les inhibiteurs de l'ECA et les antagonistes du calcium. *Hypertens Can* 1994;Septembre:3-6.
- 13. Jerome M, Xakellis GC, Angstman G, Patchin W. Initial medication selection for treatment of hypertension in an open-panel HMO. *J Am Board Fam Pract* 1995;8:1-6.
- 14. Troein M, Arneson T, Rastam L, Pirie PL, Selander S, Luepker RV. Reported treatment of hypertension by family physicians in Sweden and Minnesota: a physician survey of practice habits. *J Intern Med* 1995;238:215-21.
- 15. Weiland SK, Keil U, Spelsberg A, Hense HW, Hartel U, Gefeller O, et al. Diagnosis and management of hypertension by physicians in the Federal Republic of Germany. *J Hypertens* 1991;9:131-4.

- 16. Arroll B, Jenkins S, North D, Kearns R. Management of hypertension and the core services guidelines: results from interviews with 100 Auckland general practitioners. N Z Med J 1995;108:55-7.
- 17. Johannesson M, Borgquist L, Jonsson B. The costs of treating hypertension in Sweden. An empirical investigation in primary care. *Scand J Prim Health Care* 1991;9:155-60.
- 18. Dickerson JE, Garratt CJ, Brown MJ. Management of hypertension in general practice: agreements with and variations from the British Hypertension Society guidelines. *J Hum Hypertens* 1995;9:835-9.
- 19. Sinclair BL, Ashton T, Jackson R, Beaglehole R. Trends in antihypertensive medication costs in a cohort of Aucklanders 1982-87. *NZ Med J* 1989;102:521-3.
- 20. Adamson TE, Rodnick JE, Guillion DS. Family physicians and general internists: do they treat hypertensive patients differently? *I Fam Pract* 1989;29:93-9.
- 21. Reeves RA, Fodor G, Gryje CI, Patterson C, Spence D. Report of the Canadian Hypertension Society Consensus Conference: 4. Hypertension in the elderly. *Can Med Assoc J* 1993;149:815-20.
- 22. Dawson KG, McKenzie JK, Ross SA, Chiasson J-L, Hamet P. Report of the Canadian Hypertension Society Consensus Conference: 5. Hypertension and diabetes. *Can Med Assoc J* 1993;149:821-6.
- 23. Aubin M, Vezina L, Fortin JP, Bernard PM. Effectiveness of a program to improve hypertension screening in primary care. *Can Med Assoc J* 1994;150:509-15.
- Romm FJ, Putnam SM. The validity of the medical record. *Med Care* 1981;19:310-5.
- 25. Gong L, Zhang W, Zhu Y, Zhu J, Kong D, Pagé V, et al. Shanghai trial of nifedipine in the elderly (STONE). J Hypertens 1996;14:1237-45.
- Beto JA, Bansal VK. Quality of life in treatment of hypertension. A metaanalysis of clinical trials. Am J Hypertens 1992;5:125-33.
- 27. Boissel JP, Collet JP, Lion L, Ducruet T, Moleur P, Luciani J, et al. A randomized comparison of the effect of four antihypertensive monotherapies on the subjective quality of life in previously untreated asymptomatic patients: field trial in general practice. *J Hypertens* 1995;13:1059-67.
- 28. Palmer AJ, Fletcher AE, Rudge PJ, Andrews CD, Callaghan TS, Bulpitt CJ, et al. Quality of life in hypertensives treated with atenolol or captopril: a double-blind crossover trial. *J Hypertens* 1992;10:1409-16.

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