Missed opportunities for the secondary prevention of cardiovascular disease in Canada

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BACKGROUND: Strong evidence supports the use of antithrombotic agents (antiplatelets or oral anticoagulants), statins and angiotensin-converting enzyme inhibitors in patients with atherosclerotic cardiovascular disease; beta-blockers are additionally indicated in patients with coronary artery disease.

OBJECTIVES: The investigators sought to determine the extent to which guideline-recommended treatments and target goals are adopted in ambulatory patients with cardiovascular disease in Canada.

METHODS: Two large, prospective, community-based registries (the Vascular Protection Registry and the Guideline Oriented Approach to Lipid Lowering Registry) enrolled 9809 outpatients with coronary artery disease, cerebrovascular disease, peripheral vascular disease or multiple cardiovascular risk factors from primary care settings in nine provinces across Canada between 2001 and 2004. This analysis focused primarily on patients with cardiovascular disease (n=6296).

RESULTS: At baseline, antithrombotics, statins and angiotensin-converting enzyme inhibitors were used in 92%, 80% and 57% of patients, respectively; beta-blockers were used in 59% of patients with coronary artery disease. The dosing of most drug therapies was suboptimal compared with guideline-recommended dosing derived from clinical trials. Treatment goals for cardiovascular risk factors were suboptimally attained: low-density lipoprotein cholesterol in 50% of patients, total to high-density lipoprotein cholesterol ratio in 51% of patients, systolic and diastolic blood pressure in 58% and 78% of patients, respectively, and waist circumference and body mass index in 45% and 19%, respectively.

CONCLUSIONS: These data suggest specific opportunities for improving the care of patients with cardiovascular disease in Canada. The focus must now shift from awareness of treatment gaps to implementation of effective solutions.

Key Words: Atherosclerosis; Health care delivery; Prevention; Registries

The contemporary management of patients with atherosclerotic cardiovascular disease involves three broad therapeutic strategies. At the most fundamental level, all patients are encouraged to modify unhealthy lifestyle elements and quit smoking, attain an optimal body weight, adopt a prudent diet and exercise (1). Second, a medical regimen consisting of several secondary prevention therapies is prescribed, typically an antiplatelet agent (or oral anticoagulant), a 3-hydroxy-3-methylglutaryl coenzyme A

Prévention secondaire des maladies cardiovasculaires au Canada : Occasions manquées pour la

HISTORIQUE : Des preuves irréfutables appuient l'utilisation des antithrombotiques (antiplaquettaires ou anticoagulants oraux), des statines et des inhibiteurs de l'enzyme de conversion de l'angiotensine chez les patients souffrant de maladie cardiovasculaire athéroscléreuse. Les bêta-bloquants sont également indiqués chez les patients qui souffrent de maladie coronarienne.

OBJECTIFS : Les investigateurs ont tenté de déterminer dans quelle mesure les traitements et objectifs émanant de lignes directrices sont appliqués chez les patients non hospitalisés atteints de maladie cardiovasculaire au Canada.

MÉTHODES : Deux grands registres prospectifs basés dans la communauté (le *Vascular Protection Registry* et le *Guideline Oriented Approach to Lipid Lowering Registry*) ont inscrit 9 809 patients non hospitalisés souffrant de coronaropathie, de maladie vasculaire cérébrale, de maladie vasculaire périphérique ou de facteurs de risque cardiovasculaires multiples, soignés en médecine de premier recours dans neuf provinces du Canada entre 2001 et 2004. Cette analyse s'est principalement attardée aux patients atteints de maladie cardiovasculaire (n = 6 296).

RÉSULTATS : Au départ, les antithrombotiques, les statines et les inhibiteurs de l'enzyme de conversion de l'angiotensine étaient utilisés chez 92 %, 80 % et 57 % des patients, respectivement. Les bêta-bloquants étaient utilisés chez 59 % des patients atteints de coronaropathie. La posologie de la plupart des traitements médicamenteux était sous-optimale comparativement aux posologies préconisées dans les lignes directrices et déterminées à partir d'essais cliniques. Les objectifs thérapeutiques dans le cas des facteurs de risque cardiovasculaires ont également été plus ou moins atteints : cholestérol-LDL chez 50 % des patients, rapport cholestérol total:cholestérol-HDL chez 51 % des patients, tension artérielle systolique et diastolique chez 58 % et 78 % des patients, respectivement, et tour de taille et indice de masse corporelle, chez 45 % et 19 % des patients, respectivement.

CONCLUSIONS : Ces données illustrent les secteurs spécifiques où il y a lieu d'améliorer les soins aux patients atteints de maladie cardiovasculaire au Canada. Il faut maintenant dépasser le stade de la sensibilisation aux lacunes thérapeutiques pour appliquer des solutions efficaces.

reductase inhibitor (statin), an angiotensin-converting enzyme (ACE) inhibitor, and additionally, in patients with coronary artery disease (CAD), a beta-blocker. As with lifestyle modification, a large and persuasive body of evidence supports the provision of each of these therapies for the prevention of recurrent cardiovascular events (2-7). Finally, certain patients may also benefit from an arterial revascularization procedure to alleviate symptoms, improve prognosis or both (8,9).

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Of increasing concern is the gap between 'best medical therapy' – as reflected by evidence-based guidelines, meta-analyses and randomized trials – and actual practice patterns (10). We sought to quantify this gap in patients with stable cardiovascular disease treated in outpatient settings across Canada. Specifically, we combined data from two contemporary, community-based registries: the Vascular Protection (VP) Registry and the Guideline Oriented Approach to Lipid Lowering (GOALL) Registry. Both registries studied patients with cardiovascular disease or major cardiovascular risk factors from primary care settings, with enrolment occurring between 2001 and 2004. We focused on patients with cardiovascular disease because such individuals generally have the strongest indications for the institution of preventive therapies (11).

METHODS

Registries

The VP and GOALL Registries are prospective, practice-based registries designed and implemented by the Canadian Heart Research Centre (CHRC) to monitor outpatient clinical management practices and outcomes in populations at elevated risk for vascular events. The CHRC is a federally incorporated, nonprofit, academic research organization involved in the design and execution of patient registries and controlled clinical trials. The registries were conceived, designed and managed entirely by the CHRC.

Physicians from across Canada were directly invited to participate in the VP and GOALL Registries through mail and fax campaigns, accredited attendance at local and national continuing medical education events and scientific meetings, and from participation in prior or ongoing CHRC registries. Physicians were invited to participate without regard to their prescribing patterns, and received \$75 to \$100 (per case) for enrolling patients, completing case report forms (CRFs), obtaining follow-up information and responding to queries. Participating physicians were instructed to enroll consecutive patients. The period of accrual was December 2001 to November 2004 for VP and December 2002 to December 2004 for GOALL. Participation by patients was entirely voluntary, and all patients signed an informed consent form. The study was approved by an independent ethics review board.

Inclusion criteria

Both registries had similar, broad inclusion criteria and no exclusion criteria. Patients were eligible for enrolment if they possessed one or more of the following physician-documented diagnoses: CAD, cerebrovascular disease (CVD), peripheral vascular disease (PVD), diabetes mellitus or multiple cardiovascular risk factors.

All analyses in the present report focus on patients with cardiovascular disease (CAD, CVD or PVD). CAD was defined as the presence of at least one of the following criteria: previous myocardial infarction, unstable angina, coronary revascularization (coronary artery bypass surgery or percutaneous coronary intervention), or stable angina with either an angiogram showing greater than 50% stenosis in one or more major coronary artery or a stress test positive for ischemia. CVD was defined as a documented history of ischemic stroke or transient ischemic attack. PVD was defined as a history of intermittent claudication, or a documented decrease in pulses or bruits supported by a Doppler-based ankle-brachial index of less than 0.9 or a duplex ultrasound diagnosis (greater than 50% stenosis in one or more major peripheral artery).

Data collection

All data were collected by participating physicians who completed a standardized baseline CRF and returned it to the CHRC for data entry. Baseline information included patient demographics,

clinical variables, historical information, complete medication profiles and routine laboratory values. Patients were then followed up at six and 12 months by their physicians as part of routine clinical care, at which time another CRF was completed to assess cardiovascular outcomes. Treating physicians verified outcomes using standardized definitions provided by the CHRC. The following outcomes were recorded along with corresponding dates: myocardial infarction, unstable angina, coronary artery bypass grafting, percutaneous coronary intervention, stroke, transient ischemic attack and death (all-cause). Completed CRFs were scanned into a central electronic database using Teleform version 7.0 (Cardiff Software Inc, USA). Quality control measures ensured that queries regarding incomplete or unclear data were returned to sites for necessary correction or clarification.

Statistical analysis

The primary analysis focused on the use of antithrombotics (antiplatelets or oral anticoagulants), statins, beta-blockers and ACE inhibitors in the registries at the time of enrolment. The extent to which seven target goals for risk factor treatment were met was assessed. According to prevailing national practice guidelines, these goals included systolic blood pressure of less than 140 mmHg (less than 130 mmHg in patients with concomitant diabetes or chronic renal disease), diastolic blood pressure of less than 90 mmHg (less than 80 mmHg in patients with concomitant diabetes or chronic renal disease), low-density lipoprotein cholesterol (LDL-C) level of less than 2.5 mmol/L, total to high-density lipoprotein cholesterol (HDL-C) ratio of less than 4, triglyceride level of less than 2.0 mmol/L, body mass index between 20.0 kg/m² and 25.0 kg/m², as well as waist circumference of less than 102 cm in men and less than 88 cm in women (12-14). All of the analyses for these results were performed on baseline data.

Because preliminary analysis revealed a significant shortfall in the use of ACE inhibitors in particular, several additional analyses were performed to account for this finding. First, the use of ACE inhibitors was assessed in a well-defined, evidence-based subgroup of patients defined as having cardiovascular disease plus at least one additional indication for ACE inhibitor therapy, namely, diabetes mellitus, chronic heart failure, hypertension or chronic renal insufficiency (Cockcroft-Gault calculated creatinine clearance of less than 60 mL/min/1.73 m²) (14-17). Second, logistic regression was used to assess univariate predictors of treatment with ACE inhibitors in the overall secondary prevention cohort. Variables that were significant in univariate models ($P < 0.05$) were entered into a multiple logistic regression model using forward entry to determine independent predictors of use. This model was further adjusted for age, sex and practice province. Finally, the number of deaths, myocardial infarctions, strokes and coronary revascularizations that may be prevented over a five-year period if ACE inhibitors were extended to patients who were not prescribed this therapy were estimated. This analysis was performed by applying the appropriate RR reductions from published meta-analyses to the incidence of the corresponding outcomes seen in patients not treated with ACE inhibitors (4,5). The pooled RR for death, myocardial infarction, stroke and coronary revascularization derived from these meta-analyses were 0.88, 0.80, 0.72 and 0.86, respectively (all significant, at $P < 0.05$).

All values were summarized as percentages for categorical variables and medians (with interquartile range) for continuous variables. All tests were two-sided and considered to be significant at $P < 0.05$. Statistical analysis was carried out using SAS version 8.2 (SAS Institute Inc, USA) and SPSS version 12.0 (SPSS Inc, USA).

TABLE 1
Baseline characteristics of patients with cardiovascular disease in the Vascular Protection and Guideline Oriented Approach to Lipid Lowering Registries (n=6296)

Characteristic	Summary measure
Demographic factors	
Age, years (interquartile range)	68 (59, 75)
Sex, n (% female)	1903 (30)
Inclusion criteria, n (%)	
Coronary artery disease	5170 (82)
Myocardial infarction	2880 (46)
Unstable angina	1831 (29)
Coronary artery bypass grafting	1550 (25)
Percutaneous coronary intervention	1219 (19)
Stable angina	2205 (35)
Peripheral vascular disease	1120 (18)
Cerebrovascular disease	1391 (22)
Stroke	719 (11)
Transient ischemic attack	759 (12)
Risk factors and other comorbidities, n (%)	
Heart failure	723 (12)
Family history of premature coronary artery disease	2372 (38)
Recent cardiovascular hospitalization*	791 (13)
Hypertension	3409 (54)
Diabetes mellitus	2319 (37)
Renal insufficiency	1808 (29)
Heavy alcohol intake†	233 (4)
Current smoking	757 (19)‡
Clinical variables, median (interquartile range)	
Heart rate, beats/min	70 (64, 76)
Systolic blood pressure, mmHg	130 (120, 140)
Diastolic blood pressure, mmHg	78 (70, 80)
Body mass index, kg/m ²	28.4 (25.5, 32.0)
Waist circumference, cm	100 (91, 108)
Laboratory data, median (interquartile range)	
Total cholesterol, mmol/L	4.52 (3.91, 5.30)
Triglycerides, mmol/L	1.61 (1.18, 2.29)
High-density lipoprotein cholesterol, mmol/L	1.14 (0.96, 1.37)
Low-density lipoprotein cholesterol, mmol/L	2.49 (2.00, 3.13)
Total to high-density lipoprotein cholesterol ratio	3.96 (3.20, 4.82)
Serum glucose, mmol/L	5.80 (5.20, 7.10)
Serum creatinine, µmol/L	91 (79, 106)

All patients were enrolled between 2001 and 2004. *Admission to hospital for cardiovascular causes in the six-month interval preceding enrolment; †More than 10 alcoholic drinks per week; ‡Based on data collection in the Goal Oriented Approach to Lipid Lowering Registry (n=2829) and the diabetic cohort in the Vascular Protection Registry (n=1242)

RESULTS

A total of 9809 patients from nine Canadian provinces were enrolled by 484 physicians in the VP and GOALL Registries. The sole province that did not contribute data was Prince Edward Island. All physicians involved with enrolment in GOALL were family physicians and general practitioners, as were the majority of physicians who participated in VP (95%). Slightly fewer than one-half of patients (44%) lived in major metropolitan areas, with the remainder (56%) residing in semirural or rural locales.

Overall, 6296 patients had one or more manifestations of cardiovascular disease, and these patients formed the study cohort

TABLE 2
Rates of medication use at baseline (n=6296)

Medication use	
Antithrombotic drug	5791 (92)
Acetylsalicylic acid	5043 (80)
Ticlopidine or clopidogrel	763 (12)
Oral anticoagulant	582 (9)
Lipid-lowering drug	5349 (85)
Statin	5024 (80)
Other lipid-lowering drug*	584 (9)
Angiotensin-converting enzyme inhibitor	3558 (57)
Angiotensin receptor blocker	1093 (17)
Beta-blocker	3287 (52)
Calcium channel blocker	1930 (31)
Diuretic†	2047 (33)
Insulin	369 (6)
Oral hypoglycemic agent	1522 (24)
Estrogen replacement therapy	161 (3)

*Bile acid sequestrant, fibric acid derivative, niacin or ezetimibe; †Includes thiazide and nonthiazide diuretics

(Table 1). CAD was present in 5170 patients (82%), CVD in 1391 (22%), PVD in 1120 (18%) and there was involvement of more than one vascular bed in 1199 (19%). Major comorbidities were frequent, including hypertension (54%), diabetes mellitus (37%), renal insufficiency (29%) and chronic heart failure (12%).

High rates of antithrombotic and statin use were found in the secondary prevention cohort (Table 2). Ninety-two per cent of patients were treated with an antiplatelet or oral anticoagulant and 80% received a statin. The proportion of patients on any lipid-lowering agent was 85%. On the other hand, only 57% received an ACE inhibitor and only 59% of patients with CAD received a beta-blocker.

Overall, 4530 patients (72%) were ideal candidates for ACE inhibitor therapy (cardiovascular disease plus diabetes, heart failure, renal insufficiency and/or hypertension). In this high-risk subgroup, the use of ACE inhibitors was still only 59%. In a multivariate model, several factors independently predicted greater ACE inhibitor use: history of myocardial infarction (OR 1.32; $P<0.001$), hypertension (OR 1.29; $P<0.001$), heart failure (OR 1.46; $P<0.001$), diabetes (OR 1.43; $P<0.001$), previous percutaneous coronary intervention (OR 1.23; $P=0.005$) and recent cardiovascular hospitalization (OR 1.40; $P<0.001$). Conversely, older individuals (OR 0.95 per decade; $P=0.036$), patients with CVD (OR 0.87; $P=0.047$) and women (OR 0.72; $P<0.001$) were less likely to receive ACE inhibitor therapy. No other variable, including smoking status, locale or any other comorbid condition, predicted the use of ACE inhibitors. Analyses of use stratified by age, sex and locale are provided in Table 3. Separate analyses of use in men and women are provided in Table 4. Province-specific models gave similar results.

Suboptimal attainment of the guideline-recommended goals for cardiovascular risk factors was also found (Tables 4 and 5). In particular, only one-half of patients had their LDL-C or total to HDL-C ratio controlled to target levels. Systolic blood pressure control was achieved in only 59% of patients. Among patients with a history of hypertension, systolic and diastolic blood pressure goals were achieved in 44% and 67%, respectively. Body mass index and waist circumference goals were attained in only 19% and 45% of patients, respectively. Of note, the median dose prescribed for most

TABLE 3
Stratified analyses for angiotensin-converting enzyme inhibitor use at baseline

Characteristic	Use, n (%)	P
Age, years		<0.001
<66	1533 (57.8)	
66–74	1135 (57.7)	
75–84	759 (53.2)	
≥85	98 (52.1)	
Sex		<0.001
Male	2578 (59.4)	
Female	942 (50.1)	
Location		0.14
Urban	1578 (57.5)	
Rural	1980 (55.7)	

TABLE 4
Predictive models for current angiotensin-converting enzyme inhibitor use in men and women

Characteristic	OR*	P
Female sex (n=1799)		
Age (per decade)	1.00	0.91
Recent cardiovascular hospitalization	1.77	<0.001
Hypertension	1.26	0.035
Diabetes mellitus	1.35	0.006
Prior myocardial infarction	1.37	0.003
Percutaneous coronary intervention	1.43	0.011
Men (n=4153)		
Age (per decade)	0.92	0.005
Recent cardiovascular hospitalization	1.29	0.014
Hypertension	1.29	<0.001
Diabetes mellitus	1.50	<0.001
Prior myocardial infarction	1.35	<0.001
Percutaneous coronary intervention	1.20	0.026

*Based on a multivariable logistic regression model. Only statistically significant variables are shown. Patients with missing data were excluded from the analysis

statins and ACE inhibitors was only 25% to 50% of the target dose used in long-term clinical trials (Tables 5 and 6).

At the time of analysis, follow-up case report forms were available for 89% of the secondary prevention cohort (n=5622). In total, 482 patients (8.6%) suffered an adverse cardiovascular event during a mean follow-up of 9.4±3.6 months, equal to a rate of 115 events per 1000 patient-years at risk. The most frequent outcomes seen were unstable angina (3.1%), coronary revascularization (2.9%) and death (1.6%). The traditional composite end point of death, myocardial infarction and stroke occurred at a rate of 42 events per 1000 patient-years. It was calculated that the extension of ACE inhibitor therapy to all patients might prevent 30 deaths, 33 myocardial infarctions, 35 strokes and 65 coronary revascularizations over a five-year period, for a total of 163 events prevented.

DISCUSSION

Patient registries are an important tool for bridging the gap between evidence-based medicine and clinical practice (18). In comparison with controlled clinical trials, community-based

TABLE 5
Attainment of risk factor treatment goals at baseline (n=6296)

Risk factor	Treatment goal	Goal attainment, n (%)
Lipids		
LDL-C	<2.5 mmol/L	3151 (50)
Total to HDL-C ratio	<4	3211 (51)
Triglycerides	<2.0 mmol/L	4172 (66)
Blood pressure		
Systolic blood pressure	<140 mmHg*	3684 (59)
Diastolic blood pressure	<90 mmHg*	4914 (78)
Weight		
Body mass index	20.0 kg/m ² –25.0 kg/m ²	1188 (19)
Waist circumference	Women <88 cm, men <102 cm	2801 (45)

*Lower than 130 mmHg (systolic) and lower than 80 mmHg (diastolic) in patients with diabetes, chronic renal disease or both. HDL-C High-density lipoprotein cholesterol; LDL-C Low-density lipoprotein cholesterol

TABLE 6
Medication dosing at baseline compared with usual clinical trial dosing (n=6296)

Medication	Total daily dose, mg (median, IQR)	% of usual trial dose (reference)*
Statins		
Atorvastatin	20 (10, 20)	25 (39)
Fluvastatin	40 (20, 40)	50 (40)
Lovastatin	20 (20, 40)	50 (41)
Pravastatin	20 (20, 40)	50 (42)
Rosuvastatin	10 (10, 10)	50 (43)
Simvastatin	20 (20, 40)	50 (44)
Angiotensin-converting enzyme inhibitors		
Captopril	50 (37.5, 150)	33 (45)
Cilazapril	5 (2.5, 5)	50 (46)
Enalapril	10 (10, 20)	25–50 (47)
Fosinopril	10 (10, 20)	50 (48)
Lisinopril	20 (10, 20)	50 (49)
Perindopril	4 (4, 8)	50 (50)
Quinapril	20 (10, 40)	50 (51)
Ramipril	10 (5, 10)	100 (52)
Trandolapril	2 (2, 2)	50 (53)

*Based on randomized controlled trials with cardiovascular end points. IQR Interquartile range

registries are more likely to capture patients routinely encountered in clinical care, such as those with coexisting illness, frail and elderly patients, and women. Uptake of evidence-based therapies, adherence to treatment and prognosis are three interrelated facets that are particularly suited for study in the registry setting (19). We designed and implemented the VP and GOALL Registries because of a paucity of contemporary, Canada-wide data describing the management patterns of relatively stable outpatients with a spectrum of atherosclerotic cardiovascular disorders.

The picture we describe is mixed. Eight in 10 patients were treated with a statin, and more than nine in 10 received an antiplatelet or anticoagulant agent. Conversely, fewer than two-thirds of patients with CAD were prescribed a beta-blocker and only one-half received an ACE inhibitor; use was not substantially

greater among patients with additional indications for this therapy. This latter finding was probably not due to the neutral findings of the Prevention of Events with Angiotensin-Converting Enzyme inhibitor therapy (PEACE) trial, because enrolment in both registries was virtually complete when this study was published (20). The use of ACE inhibitors to prevent major cardiovascular events and mortality in high-risk patients is supported by randomized trials enrolling diverse clinical populations, including subjects with hypertension, diabetes, chronic nephropathy, heart failure, myocardial infarction and other forms of vascular disease (21-26). Extending the use of this therapy to those not prescribed ACE inhibitors in our cohort might have prevented an additional 163 vascular events over a five-year period. This is probably an underestimate, given that aging and acquisition of risk factors tends to magnify the risk of cardiovascular events over time (27).

Reduction of cardiovascular risk factors to target levels was also suboptimal, with particular deficits seen in LDL-C, systolic blood pressure and body weight goals. One possible reason for poor achievement of target goals is the use of low doses of drug therapies in this cohort. This is corroborated by other evidence suggesting that clinical inertia may prevent patients from achieving optimal control of their risk factors, in part due to failure to up-titrate or add cardiovascular therapies over time (28,29). Others have noted that at a particular office visit, the likelihood that a patient with uncontrolled blood pressure, blood glucose or blood lipid levels will have medications started or titrated upward is lower than 20% (30). Similar or worse inertia may exist for weight control, smoking cessation and improvement of physical activity and fitness levels over time (31-33).

Our findings agree broadly with data from other sources. For example, data from a large, international registry of nearly 67,000 patients with atherosclerosis or three major cardiovascular risk factors (34) showed that 77% of patients from North American sites were prescribed a statin, 77% of patients received an antiplatelet agent and 50% of patients received an ACE inhibitor. Suboptimal blood pressure, cholesterol, body weight attainment and continued smoking were noted in 40%, 28%, 80% and 13% of patients, respectively. A recent survey of outpatients with established coronary disease in 15 European nations (35) noted similarly poor risk factor control and even lower rates of ACE inhibitor (38%) and statin (55%) use. Moreover, relatively few patients were counselled to lose weight (57%) or exercise (67%), or given information on the role of diet in lowering blood pressure (33%) or serum cholesterol (62%). The use of beta-blockers in patients with CAD has also been noted (36). Our results suggest that similar patterns of undertreatment exist in Canada.

The present study has several important limitations. First, due to the nonrandom recruitment of participating physicians, there may have been an element of selection bias in the inclusion of patients in the registries. Conversely, physicians were instructed to enrol consecutive patients. The use of intentionally broad inclusion criteria, moreover, coupled with the lack of any exclusion criteria and the sizeable number of participating physicians (n=484), make it more likely that a diverse and representative group of patients was included. Second, our analyses of treatment rates were based on physician reporting of medication profiles rather than on pharmacy records or patient interviews. This might have introduced some error, but if this is the case, it is likely to have overestimated the use of therapies by poorly adherent patients.

Third, although we did assess body mass index and waist circumference, we did not comprehensively evaluate all aspects of lifestyle modification in our cohort, such as physical activity and

diet (moreover, we did not assess referrals for cardiac rehabilitation or medication adherence). The effects of some of these components would at least partially be reflected in patient risk factor levels, which were comprehensively assessed. Fourth, we did not exclude patients with contraindications to specific therapies from our analyses, because such data are not routinely collected. Contraindications to ACE inhibitors can include bilateral renal artery stenosis, hyperkalemia and a history of angioedema, liver and muscle disease in the case of statins, and major bleeding for antithrombotic agents. Based on past research, however, contraindication rates were likely lower than 5% (37,38). Fifth, despite efforts to clarify missing data with individual physicians, some variables had missing values, ranging from no missing data for medication use to 12.4% for LDL-C. Finally, we did not track patient response rates at the individual practice level; in addition, the validity and reliability of registry data items were unknown.

CONCLUSIONS

These data suggest considerable room for improvement in the management of patients with cardiovascular disease, particularly in three major areas. First, ACE inhibitors and beta-blockers are underused in this population. Second, cardiovascular risk factors should be managed more aggressively with greater achievement of target goals. Third, up-titration of therapies to the doses proven to be effective in clinical trials is an essential element toward achieving this task.

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