

## Practice Patterns and Trends in the Use of Medical Therapy in Patients Undergoing Percutaneous Coronary Intervention in Ontario

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**Background**—Clinical guidelines emphasize medical therapy as the initial approach to the management of patients with stable coronary artery disease (CAD). However, the extent to which medical therapy is applied before and after percutaneous coronary intervention (PCI) in contemporary clinical practice is uncertain. We evaluated medication use for patients with stable CAD undergoing PCI, and assessed whether the COURAGE study altered medication use in the Canadian healthcare system.

**Methods and Results**—A population-based cohort of 23 680 older patients (>65 years old) with stable CAD undergoing PCI in Ontario between 2003 and 2010 was assembled. Optimal medical therapy (OMT) was defined as prescription for a  $\beta$ -blocker, statin, and either angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker in the 90 days before PCI, and the same medications plus thienopyridine 90 days following PCI. Prior to PCI, 8023 (33.9%) patients were receiving OMT, 11 891 (50.2%) were on suboptimal therapy, and 3766 (15.9%) were not prescribed any medications of interest. There was significant improvement in medical therapy following PCI (OMT: 11 149 [47.1%], suboptimal therapy: 11 591 [48.9%], and none: 940 [4.0%],  $P<0.001$ ). Utilization rate of OMT reduced significantly after the publication of COURAGE (34.9% before versus 32.8% after,  $P<0.001$ ). Similarly, the rate of OMT following PCI was lower in the period after publication of COURAGE (47.3% before versus 46.9% after,  $P<0.001$ ).

**Conclusions**—OMT was prescribed in about 1 in 3 patients prior to PCI and less than half after PCI. In contrast to the anticipated impact of COURAGE, we found lower rates of medication use in PCI patients after its publication. (*J Am Heart Assoc.* 2014;3:e000882 doi: 10.1161/JAHA.114.000882)

**Key Words:** optimal medical therapy • outcomes • percutaneous coronary intervention • stable coronary artery disease

Advances in medical therapy have significantly improved the prognosis of patients with stable coronary artery disease (CAD).<sup>1,2</sup> The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) study is a landmark randomized trial comparing the effectiveness of optimal medical therapy versus percutaneous coronary intervention (PCI) in patients with stable CAD.<sup>3</sup> The study showed similar rates of cardiovascular events in the overall population

and in the older patient population.<sup>3,4</sup> These results are consistent with prior studies and meta-analyses comparing medical therapy and PCI for future adverse cardiac events.<sup>5–7</sup> In addition, while the degree of angina relief was slightly higher in the PCI group, substantial improvement in angina was also seen in the medical therapy group.<sup>3</sup> Accordingly, existing clinical practice guidelines reinforce medical therapy as the initial approach to the management of patients with stable angina, and reserve PCI for patients with persistent symptoms despite optimal medical therapy.<sup>8</sup>

Despite the widespread attention to the importance of medical therapy received in the medical literature and in the lay press, a study demonstrated that there was little change in medical therapy prior to and after PCI in the United States after publication of the COURAGE trial.<sup>9</sup> There are many potential reasons why the COURAGE results may not have changed practice patterns, one of which could be due to the existing structure of the United States healthcare system, where substantial financial incentives exist to perform invasive cardiac procedures.<sup>10,11</sup> The Canadian healthcare system, in contrast, has a single-payer model where incentives to perform procedures are less. As a result, it is

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well known that Canada has lower capacity to perform coronary invasive procedures in both acute and nonacute indications as compared to the United States.<sup>12–16</sup> We theorized that physicians in Canada may be more inclined to translate current knowledge to optimize medical therapy prior to elective PCI.

We therefore sought to evaluate the practice patterns and trends in the use of optimal medical therapy in patients with stable CAD undergoing PCI and whether the publication of COURAGE changed medical therapy practice patterns in the Canadian healthcare system.

## Methods

The Cardiac Care Network of Ontario maintains a prospective clinical registry of all individuals who undergo PCI in Ontario, Canada.<sup>17</sup> All hospitals performing PCI are required to collect information on patients' clinical characteristics, as well as procedural information on the number of stents, characteristics of each stent, and location of stent placement. We conducted a retrospective cohort study by linking this registry to several population-based administrative databases, namely, the Discharge Abstract Database of the Canadian Institute for Health Information (hospital admissions), the Ontario Health Insurance Plan database (physician service claims), the Registered Persons Database (vital statistics), the Ontario Drug Benefit database (prescriptions for individuals >65 years of age), and the Canadian census.<sup>18,19</sup> These databases have been previously validated for many outcomes, exposures, and comorbidities. The linkages were performed using unique encrypted patient identifiers to protect patient confidentiality. The need for patient informed consent was waived under Ontario's health information privacy legislation.

## Study Sample

Patients aged 66 years and over with stable CAD undergoing PCI from December 1, 2003 to March 31, 2010 in Ontario were included in the study. To define a cohort of stable CAD patients for elective procedures, those with myocardial infarction, revascularization with PCI, or coronary artery bypass grafting surgery with or without valve surgery within 12 months of the index PCI were excluded. Patients admitted to the hospital with acute coronary syndromes were excluded. Patients with severe comorbidities (eg, metastatic cancer, or severe renal, liver, or pulmonary disease) within the past year were also excluded because of competing risk of death and reasons precluding optimal use of medications. Patients with potential complications for evidenced-based therapies, such as hyperkalemia or heart block were also excluded in order to accurately assess appropriate medication use. Comorbidities were identified

using the Cardiac Care Network clinical registry, and information from the Canadian Institute for Health Information Discharge Abstract Database, which is based on International Classification of Diseases 10th Revision codes.

## Ascertainment of Medical Therapy Before and After PCI

The Ontario Drug Benefits database was used to ascertain medication use before and after the index PCI for patients over 65 years of age. We assessed the use of long-acting nitrates,  $\beta$ -blockers, calcium channel blockers, statins, angiotensin-converting enzyme (ACE)-inhibitors, and angiotensin receptor blockers (ARB) prior to PCI based on prescriptions within 90 days prior to and after index PCI. In addition to those medications, thienopyridine (clopidogrel or ticlopidine) use was assessed in the 90 days following PCI (prasugrel and ticagrelor were unavailable during the study period). There is a very high (>99%) agreement rate between the Ontario Drug Benefit prescription claims record and dispensed records from pharmacy.<sup>20</sup> Aspirin use could not be formally evaluated because many patients purchase aspirin over the counter and this is not recorded in the Ontario Drug Benefits database.

## Definition of Optimal Medical Therapy

We defined "optimal medical therapy" as prescription for  $\beta$ -blocker, statin, and either ACE-inhibitor or ARB in the 90 days prior to PCI, and the same medications along with a thienopyridine in the 90 days following PCI. ACE-inhibitor or ARB use was considered in keeping with the COURAGE definition of optimal medical therapy where ACE-inhibitors or ARB were encouraged in all patients with stable CAD for secondary prevention.<sup>3</sup> Suboptimal therapy was defined as prescription for at least 1 of the above medications. No medical therapy was defined as the absence of all of these medications. Recognizing that symptomatic anginal relief is important in patients with stable angina (particularly pre-PCI), we considered an alternate definition of medical therapy based on the prescription of any 2 medications from the following in the 90 days pre-PCI:  $\beta$ -blocker, long-acting nitrate, calcium channel blocker or either ACE-inhibitor or ARB, and the same medications along with a thienopyridine and statin in the 90 days following PCI ("symptom-oriented medical therapy"). Secondary end points also included the prescription rates of individual medications.

## Statistical Analysis

We compared demographic characteristics, clinical characteristics, stratified by (1) medication use, and (2) COURAGE

publication using  $\chi^2$  tests for categorical variables and  $t$  tests for continuous variables. We used the period December 1, 2003 to March 31, 2007 for “pre-COURAGE” and July 1, 2007 to March 31, 2010 for the “post-COURAGE” period, allowing for a 3-month period for the dissemination of the trial results (COURAGE was published on March 26, 2007).

Medication prescription rates before and after PCI were compared in the overall cohort as well as in the periods before and after the publication of the COURAGE trial to examine whether the use of medical therapy changed after the publication of the COURAGE trial. Continuous variables are reported as mean $\pm$ SD and compared using  $t$  tests for normally distributed data. Categorical variables are reported as percentages and compared using the  $\chi^2$  test. The McNemar test was used to compare medical therapy use before and after the publication of the COURAGE trial.

We also used a logistic regression model to examine predictors of optimal medical therapy in the 90 days prior to the PCI. Variables considered and entered in the regression model included demographic and clinical variables such as age, sex, Canadian Cardiovascular Society angina class, prior cardiovascular disease and other comorbidities, hospital status, and procedure year. It was possible for some patients to have been referred for cardiac catheterization by primary care physicians or other physicians directly, without prior evaluation by a cardiologist or an internist on an outpatient basis, and vice versa. Thus, we included outpatient physician (primary care physician and/or cardiologist or internist) visits within the preceding 90 days in the model. PCI during the same session as the cardiac catheterization (commonly referred to as ad-hoc PCI) was not considered in this model because it does not impact on medical treatment prior to PCI.

All statistical tests are 2-sided and a  $P$ -value  $<0.01$  was considered statistically significant. All analyses were performed using SAS 9.2 (SAS Institute, Cary, NC).

## Results

The initial registry population in the study period included 122 528 PCI procedures. After excluding patients who were younger than 65 years old (68 591 patients), patients with myocardial infarction in the past year (19 216 patients), PCI or coronary artery bypass grafting surgery in the past year (6014 patients), patients with severe comorbidities or potential contraindications to medical therapy (1775 patients), and missing data, the final study population included 23 680 patients with stable CAD who received PCI from December 1, 2003 to March 31, 2010 (Figure).

## Baseline Characteristics According to Medical Therapy Prior to PCI

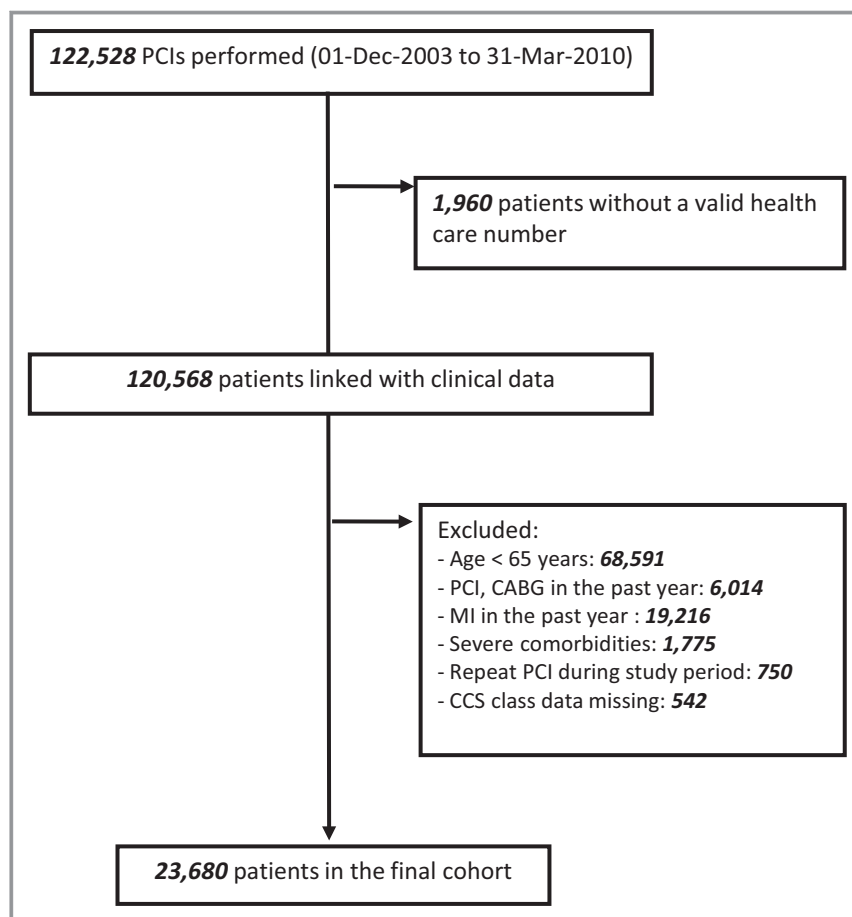
The mean age of the cohort was 74.1 years and the majority (64%) were male (Table 1). Of the 23 680 patients undergoing PCI, only 8023 patients (33.9%) were on optimal medical therapy, 11 891 (50.2%) were receiving suboptimal medical therapy, and 15.9% were not on any  $\beta$ -blocker, statin, or either ACE-inhibitor or ARB in the 90 days before the procedure. In general, patients who were receiving optimal medical therapy before their PCI had higher rates of comorbidities, prior cardiovascular disease, and to have undergone a prior stress test compared to patients who received suboptimal or no medical therapy prior to PCI, and were less likely to have moderate to severe angina (Table 1). In addition, patients on optimal medical therapy were more often evaluated by a primary care physician and/or cardiologist or an internist in an outpatient setting in the 90 days prior to PCI. For example, 86.1% of patients receiving optimal medical therapy were evaluated by a cardiologist or an internist in the 90 days prior to PCI, compared with 69.6% in the suboptimal medical therapy group, and 27.3% in the no medical therapy group. Performance of ad-hoc PCI was common (14 045 patients, 59.3%), and most commonly observed among patients not on any medical therapy prior to PCI (85.2%) as compared to those on optimal medical therapy (46.2%) (Table 1).

## Factors Associated With Optimal Medical Therapy Prior to PCI

In the multivariate analysis, younger age, lower income, remote history of revascularization, performance of stress test prior to PCI, and cardiac risk factors or conditions were associated with significantly increased likelihood of being on optimal medical therapy (Table 2). Cardiologist assessment was associated with a 2-fold increased likelihood of being on optimal medical therapy (odds ratio 2.31; 95% CI 2.12 to 2.51). Patients at lower angina classification were more likely to receive optimal therapy than patients with Canadian Cardiovascular Society class 4 angina. There was no evidence of increased use of optimal medical therapy over time. In fact, patients who received PCI in 2003–2005 (odds ratio 1.76; 95% CI 1.58 to 1.96) and 2005–2006 (odds ratio 1.6; 95% CI 1.44 to 1.79) had significantly higher likelihood of receiving optimal medical therapy compared with patients undergoing PCI in 2009–2010 (Table 2).

## Medical Therapy Before and After PCI

Medication prescription rates improved following PCI, with 8023 patients (33.9%, 95% CI, 33.3 to 34.5) receiving optimal



**Figure.** Cohort details. CABG indicates coronary artery bypass graft surgery; CCS, Canadian Cardiovascular Society; MI, myocardial infarction; PCI, percutaneous coronary intervention.

medical therapy in the 90 days prior and 11 153 patients (47.1%, 95% CI 46.5 to 47.7) receiving optimal medical therapy in the 90 days post-PCI (Table 3). Prescription rates of  $\beta$ -blockers increased significantly from 56.9% before PCI to 70.6% after PCI ( $P<0.001$ ). Similarly, prescription rates of statins (64.3% to 84.6%), ACE inhibitors or ARBs (62.3% to 74.5%), and clopidogrel (22.7% to 87.1%) increased significantly after PCI, whereas the use of long-acting nitrates (23.5% to 14.5%) and calcium-channel blockers decreased (38.8% to 30.9%), as might be expected following revascularization (Table 3).

### Medical Therapy Before and After COURAGE

A comparable number of patients underwent PCI in the period before (11 984 patients) and after (11 696 patients) publication of the COURAGE trial. Although patients were largely similar in terms of their demographic and clinical characteristics (Table 4), the rate of optimal medical therapy prior to PCI reduced slightly following COURAGE (32.8%, 95%

CI 34.1 to 35.8 after versus 34.9%, 95% CI 34.1 to 35.8 before,  $P<0.001$ ; Table 5). The rates of the individual medications prescribed before PCI were also lower or unchanged during the post-COURAGE period. Less than two thirds of the patients were on symptom-oriented medical therapy prior to PCI, and rates were lower in the post-COURAGE period (Table 5).

Similarly, the rate of optimal medical therapy following PCI was lower in the period after the COURAGE trial compared with before the trial (47.3%, 95% CI 46.4 to 48.2 before versus 46.9%, 95% CI 46.0 to 47.8 after,  $P<0.001$ ; Table 4). Rates of the individual medications prescribed after PCI were also lower or unchanged during the post-COURAGE period. Similarly, the rate of symptom-oriented medical therapy following PCI was unchanged in the post-COURAGE period (Table 6). There was no significant change in medication prescription rates after the COURAGE trial publication before or after PCI when stratified by severity of angina based on Canadian Cardiovascular Society class (Table 7).

**Table 1.** Demographic and Clinical Characteristics, Stratified by Medical Therapy 90 Days Prior to PCI

Characteristics	Total (N=23 680)	Optimal (3 Meds) (N=8023)	Suboptimal (1 or 2 Meds) (N=11 891)	None (N=3766)	P-Value
Age, y (at PCI date)	74.1±5.9	73.7±5.5	74.4±5.9	74.4±6.5	<0.001
66 to 75	14 744 (62.3%)	5219 (65.1%)	7233 (60.8%)	2292 (60.9%)	<0.001
76 to 85	7970 (33.7%)	2616 (32.6%)	4123 (34.7%)	1231 (32.7%)	
>85	966 (4.1%)	188 (2.3%)	535 (4.5%)	243 (6.5%)	
Male	15 148 (64.0%)	5299 (66.0%)	7440 (62.6%)	2409 (64.0%)	
Low income	4391 (18.5%)	1594 (19.9%)	2207 (18.6%)	590 (15.7%)	<0.001
CCS angina classification					
0	1716 (7.2%)	647 (8.1%)	894 (7.5%)	175 (4.6%)	<0.001
1	1330 (5.6%)	518 (6.5%)	716 (6.0%)	96 (2.5%)	
2	5238 (22.1%)	2313 (28.8%)	2682 (22.6%)	243 (6.5%)	
3	5862 (24.8%)	2745 (34.2%)	2868 (24.1%)	249 (6.6%)	
4	9534 (40.3%)	1800 (22.4%)	4731 (39.8%)	3003 (79.7%)	
Ad-hoc PCI	14 045 (59.3%)	3710 (46.2%)	7128 (59.9%)	3207 (85.2%)	<0.001
Prior PCI	2490 (10.5%)	1260 (15.7%)	1111 (9.3%)	119 (3.2%)	<0.001
Prior CABG	3144 (13.3%)	1732 (21.6%)	1314 (11.1%)	98 (2.6%)	<0.001
Exercise stress test	11 633 (49.1%)	5081 (63.3%)	5954 (50.1%)	598 (15.9%)	<0.001
Smoking					
Current	8253 (34.9%)	2900 (36.1%)	4104 (34.5%)	1249 (33.2%)	0.004
Ever	10 191 (43.0%)	3566 (44.4%)	5125 (43.1%)	1500 (39.8%)	<0.001
Hypertension	15 111 (63.8%)	5755 (71.7%)	7939 (66.8%)	1417 (37.6%)	<0.001
Diabetes	7960 (33.6%)	3542 (44.1%)	3830 (32.2%)	588 (15.6%)	<0.001
Hyperlipidemia	13 422 (56.7%)	5534 (69.0%)	6863 (57.7%)	1025 (27.2%)	<0.001
Cerebrovascular disease	2280 (9.6%)	888 (11.1%)	1195 (10.0%)	197 (5.2%)	<0.001
Congestive heart failure	2037 (8.6%)	868 (10.8%)	973 (8.2%)	196 (5.2%)	<0.001
Peripheral vascular disease	2163 (9.1%)	917 (11.4%)	1096 (9.2%)	150 (4.0%)	<0.001
Pulmonary disease	1101 (4.6%)	305 (3.8%)	628 (5.3%)	168 (4.5%)	<0.001
Other medical therapy					
Calcium channel blocker	9177 (38.8%)	3497 (43.6%)	5047 (42.4%)	633 (16.8%)	<0.001
Long-acting nitrate	5574 (23.5%)	2786 (34.7%)	2659 (22.4%)	129 (3.4%)	<0.001
Warfarin	974 (4.1%)	399 (5.0%)	503 (4.2%)	72 (1.9%)	<0.001
Teaching hospital	16 126 (68.1%)	5499 (68.5%)	8114 (68.2%)	2513 (66.7%)	0.130
PCI year					
2003–2005	3613 (100.0%)	1285 (35.6%)	1820 (50.4%)	508 (14.1%)	0.005
2005–2006	3348 (100.0%)	1165 (34.8%)	1685 (50.3%)	498 (14.9%)	
2006–2007	4155 (100.0%)	1444 (34.8%)	2053 (49.4%)	658 (15.8%)	
2007–2008	3521 (100.0%)	1190 (33.8%)	1756 (49.9%)	575 (16.3%)	
2008–2009	4209 (100.0%)	1382 (32.8%)	2125 (50.5%)	702 (16.7%)	
2009–2010	4834 (100.0%)	1557 (32.2%)	2452 (50.7%)	825 (17.1%)	
Primary care physician visit*	18 357 (77.5%)	6584 (82.1%)	9527 (80.1%)	2246 (59.6%)	<0.001
Cardiologist or internist visit*	16 220 (68.5%)	6910 (86.1%)	8282 (69.6%)	1028 (27.3%)	<0.001

CABG indicates coronary artery bypass graft surgery; CCS, Canadian Cardiovascular Society; PCI, percutaneous coronary intervention.

\*In the 90 days before PCI.



**Table 2.** Factors Associated With Optimal Medical Therapy Prior to PCI\*

Variables	Odds Ratio (95% CI)	P-Value
Age, y (reference >85 years)		<0.001
66 to 75	1.37 (1.15 to 1.64)	
76 to 85	1.31 (1.1 to 1.57)	
Male	1.07 (1.0 to 1.14)	0.042
Low income	1.15 (1.06 to 1.24)	<0.001
CCS angina classification (reference CCS 4)		<0.001
0 to 1	1.6 (1.44 to 1.78)	
2	1.89 (1.72 to 2.08)	
3	2.03 (1.86 to 2.23)	
Prior PCI	1.79 (1.63 to 1.97)	<0.001
Prior CABG	2.04 (1.89 to 2.22)	<0.001
Exercise stress test	1.35 (1.26 to 1.45)	<0.001
Current smoking	1.0 (0.93 to 1.06)	0.930
Hypertension	1.46 (1.36 to 1.57)	<0.001
Diabetes	1.62 (1.52 to 1.72)	<0.001
Hyperlipidemia	1.64 (1.53 to 1.77)	<0.001
Cerebrovascular disease	1.1 (1.0 to 1.22)	0.055
Congestive heart failure	1.57 (1.41 to 1.74)	<0.001
Peripheral vascular disease	1.15 (1.04 to 1.27)	0.007
Pulmonary disease	0.63 (0.55 to 0.73)	<0.001
Teaching hospital	0.98 (0.92 to 1.05)	0.620
PCI year (2009–2010 as reference)		<0.001
2003–2005	1.76 (1.58 to 1.96)	
2005–2006	1.6 (1.44 to 1.79)	
2006–2007	1.2 (1.06 to 1.29)	
2007–2008	1.15 (1.04 to 1.28)	
2008–2009	1.06 (1.05 to 1.21)	
Primary care physician visit	1.13 (1.05 to 1.21)	0.002
Cardiologist or internist visit	2.2 (2.02 to 2.41)	<0.001

CABG indicates coronary artery bypass graft surgery; CCS, Canadian Cardiovascular Society; PCI, percutaneous coronary intervention.

\*The model predicts the use of optimal medical therapy 90 days prior to PCI. The adjusted odds ratios were derived from multivariate logistic regression model. This model had a c-index (area under the receiving operating curve) of 0.74.

## Discussion

Our study provides new insights into the practice pattern of medical therapy in patients with stable angina undergoing revascularization with PCI in Canada. Our results demonstrate that only one third of patients undergoing PCI for stable coronary artery disease were prescribed optimal medical therapy with  $\beta$ -blockers, statins, and either ACE-inhibitors or

ARBs in the 90 days prior to their procedure. While medication prescription rates improved following PCI, less than half of patients were receiving optimal medical therapy in the 90 days following PCI. In addition, there was no substantial change in this practice pattern over the study period, including following the publication and dissemination of the COURAGE trial in 2007. These findings suggest that despite mounting evidence of the importance of medical therapy in patients with stable coronary disease, and the strong clinical guideline recommendations for maximizing the medical therapy prior to and in conjunction with revascularization,<sup>8</sup> most patients are still treated with inadequate medical therapy. We also found relatively low rates of use of anti-anginals such as nitrates prior to PCI even in patients with significant symptoms.

The concept of applying optimal medical therapy was endorsed in the COURAGE trial, in which  $\approx 90\%$  of the medically treated cohort was compliant with aspirin, statin, and  $\beta$ -blocker therapies at 1 year.<sup>3</sup> At 3 years, 75% of patients were on ACE inhibitors or ARBs, 92% were on a statin, and 86% were on a  $\beta$ -blocker in the medical therapy arm and similar compliance was present even in the PCI group. This is in contrast to “real world” practice, both in terms of prescription and compliance with recommended anti-anginal and preventative medical therapy. Our results are in keeping with prior large studies that have shown much lower rates of medical therapy in patients with coronary artery disease.<sup>9,21–23</sup> Borden et al showed that among patients with stable CAD undergoing PCI in the United States, less than half received optimal medical therapy prior to PCI and approximately two thirds of patients received it after discharge from the hospital following PCI, with little change after the publication of the COURAGE trial.<sup>9</sup>

We initially hypothesized that physicians may be more inclined to apply COURAGE results in the Canadian healthcare system, where there is a government-regulated single-payer model with perhaps less incentive to perform procedures and where waiting lists are traditionally longer.<sup>10,15</sup> In addition, under the Ontario Drug Benefit Program, medications are generally available with low co-payment and dispensing fees. This was expected to result in better medication prescription and adherence compared with other jurisdictions with limited medication coverage and higher co-payments. However, we found that the prescription rates of optimal medical therapy were lower in our study compared with the US study. In addition, a surprising 16% of the patients undergoing PCI had not received any cardiac medications we assessed prior to the PCI procedure.

We also found that patients with angina at higher Canadian Cardiovascular Society class were less likely to be on medical therapy prior to PCI. The reasons for this finding are not entirely clear, although it is possible that these patients had

**Table 3.** Medication Prescription Rates Before and After PCI

Medication	No. (%), (95% CI) of Patients		P-Value
	Pre-PCI (90 Days)	Post-PCI (90 Days)	
Optimal medical therapy	33.9 (33.3 to 34.5)	47.1 (46.5 to 47.7)	<0.001
Suboptimal medical therapy	50.2 (49.6 to 50.9)	48.9 (48.3 to 49.6)	0.001
None	15.9 (15.4 to 16.4)	4.0 (3.7 to 4.2)	<0.001
Individual medications			
Long-acting nitrate	23.5 (23.0 to 24.1)	14.5 (14.0 to 14.9)	<0.001
β-Blocker	56.9 (56.2 to 57.5)	70.6 (70.1 to 71.2)	<0.001
Calcium channel blocker	38.8 (38.1 to 39.4)	30.9 (30.3 to 31.5)	<0.001
Statin	64.3 (63.6 to 64.9)	84.6 (84.1 to 85.0)	<0.001
ACE-I/ARB	62.3 (61.7 to 63.0)	74.5 (73.9 to 75.0)	<0.001
Clopidogrel	22.7 (22.1 to 23.2)	87.1 (86.7 to 87.5)	<0.001
Symptom-oriented medical therapy	61.2 (60.6 to 61.8)	57.9 (57.3 to 58.5)	<0.001

Optimal medical therapy is defined as prescription for β-blocker, statin, and either ACE inhibitor or ARB in the 90 days prior to PCI, and the same medications along with a thienopyridine in the 90 days following PCI. Suboptimal therapy is defined as prescription of at least 1 of the above individual medications. Symptom-oriented medical therapy is defined as prescription of any 2 medications from the following in the 90 days pre-PCI: β-blocker, long-acting nitrate, calcium channel blocker or either ACE inhibitor or ARB, and the same medications along with a thienopyridine and statin in the 90 days following PCI. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; PCI, percutaneous coronary intervention.

more symptoms given the lack of appropriate medical therapy prior to PCI. An alternative explanation may be that physicians want to refer these patients for more urgent catheterization and PCI, given the severity of their symptoms even before instituting appropriate medical therapy, although there is little justification for such an approach.

There are several possible reasons why medical therapy is underprescribed in patients with stable CAD and why the COURAGE trial results have not been implemented in common clinical practice. First, it has been shown that patients overestimate the benefits of PCI by believing that PCI would prevent myocardial infarction or fatality.<sup>24</sup> Such belief may lead to a desire of a “quick-fix” for their symptoms rather than to comply with a daily medication regimen for a long period of time. Second, physicians may not universally accept the results of recent trials, such as COURAGE, or there may be a knowledge gap regarding appropriate management of patients with stable CAD, believing that PCI is better compared to medical therapy.<sup>25</sup> For example, a recent study indicates that about 20% of cardiologists still believe that the PCI may reduce death or prevent myocardial infarction in stable CAD patients.<sup>24</sup> Third, we found that many patients who were on suboptimal or no therapy received PCI as an ad-hoc procedure. The reasons for such high rates of ad-hoc PCI are likely multifactorial. From the patient’s perspective, combining the diagnostic angiogram and the intervention in a single setting is convenient, and this approach forms part of both patients’ and physicians’ expectations. It is also possible that physicians and patients may be more inclined to undertake ad-hoc PCI rather than prescribe medical therapy and delay any

revascularization, given the severity of their patients’ symptoms. Nevertheless, while ad-hoc PCI may be more acceptable in the acute coronary syndrome setting where PCI improves outcomes, delayed or non-ad-hoc PCI may be preferable in patients with stable angina.<sup>26</sup> This allows for a proper and frank discussion of all therapeutic options in a more relaxed setting, including optimization or intensification of medical therapy.

Our study adds to the growing literature indicating suboptimal use of proven therapies in practice and has important implications for the contemporary management of patients with stable CAD. Current practice guidelines recommend optimizing medical therapy for improvement of symptoms and prognosis prior to consideration of revascularization. Improved utilization of medications is a significant opportunity for improvement in health care of patients with cardiovascular disease. Revascularization may be safely deferred or may not be required in patients appropriately treated with medical therapy, thereby reducing societal costs at the same time as improving survival. Our study reinforces the importance of appropriateness criteria for coronary revascularization. Indeed, policy makers and insurers may eventually mandate the need for appropriate and aggressive medical therapy before reimbursing PCI procedures.

Our study has several important limitations. First, we did not assess prescription of aspirin because we were unable to capture this medication in the Ontario Drug Benefits database because many patients purchase aspirin over the counter rather than through the drug benefit program. Second, our study was limited to an older cohort >65 years

**Table 4.** Demographic and Clinical Characteristics Before and After Publication of COURAGE

Characteristics	Total (N=23 680)	Pre-COURAGE (N=11 984)	Post-COURAGE (N=11 696)	P-Value
Age, y (at PCI date)	74.1±5.9	73.8±5.6	74.4±6.1	<0.001
Age group, y				
66 to 75	14 744 (62.3%)	7714 (64.4%)	7030 (60.1%)	<0.001
76 to 85	7970 (33.7%)	3910 (32.6%)	4060 (34.7%)	
>85	966 (4.1%)	360 (3.0%)	606 (5.2%)	
Male	15 148 (64.0%)	7692 (64.2%)	7456 (63.7%)	0.483
Low income	4391 (18.5%)	2300 (19.2%)	2091 (17.9%)	0.009
CCS angina classification				
0	1716 (7.2%)	913 (7.6%)	803 (6.9%)	<0.001
1	1330 (5.6%)	685 (5.7%)	645 (5.5%)	
2	5238 (22.1%)	2625 (21.9%)	2613 (22.3%)	
3	5862 (24.8%)	3386 (28.3%)	2476 (21.2%)	
4	9534 (40.3%)	4375 (36.5%)	5159 (44.1%)	
Ad-hoc PCI	14 045 (59.3%)	6495 (54.2%)	7550 (64.6%)	<0.001
Prior PCI	2490 (10.5%)	922 (7.7%)	1568 (13.4%)	<0.001
Prior CABG	3144 (13.3%)	1537 (12.8%)	1607 (13.7%)	0.038
Exercise stress test	11 633 (49.1%)	6214 (51.9%)	5419 (46.3%)	<0.001
Smoking				
Current	8253 (34.9%)	5107 (42.6%)	3146 (26.9%)	<0.001
Ever	10 191 (43.0%)	5107 (42.6%)	5084 (43.5%)	0.185
Hypertension	15 111 (63.8%)	6548 (54.6%)	8563 (73.2%)	<0.001
Diabetes	7960 (33.6%)	3800 (31.7%)	4160 (35.6%)	<0.001
Hyperlipidemia	13 422 (56.7%)	5472 (45.7%)	7950 (68.0%)	<0.001
Cerebrovascular Disease	2280 (9.6%)	1183 (9.9%)	1097 (9.4%)	0.199
Congestive heart failure	2037 (8.6%)	977 (8.2%)	1060 (9.1%)	0.012
Peripheral vascular disease	2163 (9.1%)	1133 (9.5%)	1030 (8.8%)	0.084
Pulmonary disease	1101 (4.6%)	490 (4.1%)	611 (5.2%)	<0.001
Other medical therapy				
Calcium channel blocker	9177 (38.8%)	4688 (39.1%)	4489 (38.4%)	0.244
Long-acting nitrate	5574 (23.5%)	3209 (26.8%)	2365 (20.2%)	<0.001
Warfarin	974 (4.1%)	359 (3.0%)	615 (5.3%)	<0.001
Teaching hospital	16 126 (68.1%)	8404 (70.1%)	7722 (66.0%)	<0.001
Primary care physician visit	18 357 (77.5%)	9458 (78.9%)	8899 (76.1%)	<0.001
Cardiologist or internist visit	16 220 (68.5%)	8343 (69.6%)	7877 (67.3%)	<0.001

CABG indicates coronary artery bypass graft surgery; CCS, Canadian Cardiovascular Society; COURAGE, Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation; PCI, percutaneous coronary intervention.

of age) because we did not have information on prescriptions for younger patients. However, the elderly population represents a high-risk group with higher baseline cardiovascular risk profile and derives equal if not more benefit from medical therapy as younger patients. Third, medication prescription was used as a surrogate for medication use and compliance, and we were unable to determine whether

patients actually took their medication once it was dispensed. However, this misclassification bias would tend to overestimate medication use. Fourth, we were unable to control for all factors that might influence a physician’s decision to prescribe (or not prescribe) medications, or fully define contraindications to therapy with these medications, which could underestimate optimal medical therapy use.



**Table 5.** Medication Prescription Rates Before and After Publication of COURAGE in the 90 Days Prior to PCI

Medication	Total	No. (%), (95% CI) of patients		P-Value*
		Pre-COURAGE	Post-COURAGE	
<b>Pre-PCI</b>				
Optimal medical therapy	8023 (33.9%)	34.9 (34.1 to 35.8)	32.8 (31.9 to 33.6)	<0.001
Suboptimal medical therapy	11 891 (50.2%)	50.0 (49.1 to 50.9)	50.4 (49.5 to 51.3)	0.519
None	3766 (15.9%)	15.0 (14.4 to 15.7)	16.8 (16.1 to 17.5)	<0.001
<b>Individual medications</b>				
Long-acting nitrate	5574 (23.5%)	26.8 (26.0 to 27.6)	20.2 (19.5 to 21.0)	<0.001
β-Blocker	13 467 (56.9%)	59.3 (58.4 to 60.2)	54.4 (53.5 to 55.3)	<0.001
Calcium channel blocker	9177 (38.8%)	39.1 (38.3 to 40.0)	38.4 (37.5 to 39.3)	0.244
Statin	15 215 (64.3%)	64.3 (63.5 to 65.2)	64.2 (63.3 to 65.0)	0.787
ACE-I/ARB	14 762 (62.3%)	62.7 (61.9 to 63.6)	61.9 (61.1 to 62.8)	0.205
Clopidogrel	5366 (22.7%)	23.6 (22.8 to 24.3)	21.7 (21.0 to 22.5)	<0.001
Symptom-oriented medical therapy	61.2 (60.6, 61.8)	63.6 (62.8 to 64.5)	58.7 (57.8 to 59.6)	<0.001

Optimal medical therapy is defined as prescription for β-blocker, statin, and either ACE inhibitor or ARB in the 90 days prior to PCI. Suboptimal therapy is defined as prescription of at least 1 of the above individual medications. Symptom-oriented medical therapy is defined as the prescription of any 2 medications from the following in the 90 days pre-PCI: β-blocker, long-acting nitrate, calcium channel blocker or either ACE inhibitor or ARB. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; COURAGE, Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation; PCI, percutaneous coronary intervention.

\*McNemar test.

While it is possible that we have not captured all contraindications to therapy, this is unlikely to be different in the period before or after the COURAGE trial, thus not altering the finding that optimal medical therapy use did not differ after COURAGE. Finally, our data are from Ontario and may

not reflect prescribing practices from other areas. However, Ontario is the largest province and encompasses a third of the Canadian population.

In conclusion, we found that among patients with stable CAD undergoing PCI, only a third of patients were prescribed

**Table 6.** Medication Prescription Rates Before and After Publication of COURAGE in the 90 Days After PCI

Medication	Total	No. (%), (95% CI) of patients		P-Value*
		Pre-COURAGE	Post-COURAGE	
<b>Post-PCI</b>				
Optimal medical therapy	11 149 (47.1%)	47.3 (46.4 to 48.2)	46.9 (46.0 to 47.8)	0.520
Suboptimal medical therapy	11 591 (48.9%)	49.1 (48.2 to 50.0)	48.8 (47.9 to 49.7)	0.567
None	940 (4.0%)	3.6 (3.3 to 3.9)	4.4 (4.0 to 4.7)	0.002
<b>Individual medications</b>				
Long-acting nitrate	3426 (14.5%)	15.9 (15.2 to 16.5)	13.0 (12.4 to 13.7)	<0.001
β-Blocker	16 729 (70.6%)	71.3 (70.5 to 72.1)	70.0 (69.1 to 70.8)	0.023
Calcium channel blocker	7320 (30.9%)	31.4 (30.5 to 32.2)	30.4 (29.6 to 31.3)	0.125
Statin	20 028 (84.6%)	84.1 (83.4 to 84.8)	85.1 (84.4 to 85.7)	0.038
ACE-I/ARB	17 638 (74.5%)	75.9 (75.1 to 76.6)	73.1 (72.3 to 73.9)	<0.001
Clopidogrel	20 629 (87.1%)	86.7 (86.1 to 87.3)	87.5 (86.9 to 88.1)	0.053
Symptom-oriented medical therapy	57.9 (57.3, 58.5)	58.2 (57.3 to 59.1)	57.6 (56.7 to 58.5)	0.316

Optimal medical therapy is defined as prescription for β-blocker, statin, and either ACE inhibitor or ARB along with a thienopyridine in the 90 days following PCI. Suboptimal therapy is defined as prescription of at least 1 of the above individual medications. Symptom-oriented medical therapy is defined as the prescription of any 2 medications from the following: β-blocker, long-acting nitrate, calcium channel blocker or either ACE inhibitor or ARB, along with a thienopyridine and statin in the 90 days following PCI. ACE-I indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; COURAGE, Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation; PCI, percutaneous coronary intervention.

\*McNemar test.

**Table 7.** Medication Prescription Rates Before and After Publication of COURAGE, Stratified by Before and After PCI and CCS Class

Medication	No. (%), (95% CI) of Patients		P-Value*
	Pre-COURAGE	Post-COURAGE	
<b>CCS class 0 to 2 (N=8284)</b>			
<b>Pre-PCI</b>			
Optimal medical therapy	1775 (42.0%)	1703 (41.9%)	0.929
Suboptimal medical therapy	2151 (50.9%)	2141 (52.7%)	0.104
None	297 (7.0%)	217 (5.3%)	0.001
Nitrate	1042 (24.7%)	875 (21.5%)	<0.001
β-Blocker	2857 (67.7%)	2726 (67.1%)	0.609
Calcium channel blocker	1629 (38.6%)	1659 (40.9%)	0.034
Statin	3165 (74.9%)	3209 (79.0%)	<0.001
ACE-I/ARB	2957 (70.0%)	2848 (70.1%)	0.914
Clopidogrel	1339 (31.7%)	1347 (33.2%)	0.155
<b>Post-PCI</b>			
Optimal medical therapy	1728 (40.9%)	1560 (38.4%)	0.020
Suboptimal medical therapy	2440 (57.8%)	2455 (60.5%)	0.013
None	55 (1.3%)	46 (1.1%)	0.482
Nitrate	532 (12.6%)	487 (12.0%)	0.402
β-Blocker	2823 (66.8%)	2583 (63.6%)	0.002
Calcium channel blocker	1400 (33.2%)	1484 (36.5%)	0.001
Statin	3515 (83.2%)	3469 (85.4%)	0.006
ACE-I/ARB	3132 (74.2%)	2863 (70.5%)	<0.001
Clopidogrel	3750 (88.8%)	3677 (90.5%)	0.009
<b>CCS Class 3 to 4 (N=15 396)</b>			
<b>Pre-PCI</b>			
Optimal medical therapy	2413 (31.1%)	2132 (27.9%)	<0.001
Suboptimal medical therapy	3842 (49.5%)	3757 (49.2%)	0.713
None	1506 (19.4%)	1746 (22.9%)	<0.001
Nitrate	2167 (27.9%)	1490 (19.5%)	<0.001
β-Blocker	4249 (54.7%)	3635 (47.6%)	<0.001
Calcium channel blocker	3059 (39.4%)	2830 (37.1%)	0.003
Statin	4545 (58.6%)	4296 (56.3%)	0.004
ACE-I/ARB	4561 (58.8%)	4396 (57.6%)	0.134
Clopidogrel	1486 (19.1%)	1194 (15.6%)	<0.001
<b>Post-PCI</b>			
Optimal medical therapy	3939 (50.8%)	3922 (51.4%)	0.445
Suboptimal medical therapy	3448 (44.4%)	3248 (42.5%)	0.018
None	374 (4.8%)	465 (6.1%)	<0.001
Nitrate	1369 (17.6%)	1038 (13.6%)	<0.001
β-Blocker	5723 (73.7%)	5600 (73.3%)	0.579
Calcium channel blocker	2359 (30.4%)	2077 (27.2%)	<0.001
Statin	6563 (84.6%)	6481 (84.9%)	0.579

Continued

Table 7. Continued

Medication	No. (%), (95% CI) of Patients		P-Value*
	Pre-COURAGE	Post-COURAGE	
ACE-I/ARB	5961 (76.8%)	5682 (74.4%)	<0.001
Clopidogrel	6640 (85.6%)	6562 (85.9%)	0.488

Optimal medical therapy is defined as prescription for  $\beta$ -blocker, statin, and either ACE-inhibitor or ARB in the 90 days prior to PCI, and the same medications along with a thienopyridine in the 90 days following PCI. Suboptimal therapy is defined as prescription of at least 1 of the above individual medications.

ACE-I indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCS, Canadian Cardiovascular Society; COURAGE, Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation; PCI, percutaneous coronary intervention.

\*McNemar test.

optimal medical therapy in the 90 days prior to their procedure, and less than half were receiving optimal medical therapy in the 90 days following PCI. There was no substantial change in medical therapy prescription practice pattern over the study period, including following the publication of the COURAGE trial.

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