

Risk Factor Control for Coronary Artery Disease Secondary Prevention in Large Randomized Trials

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- Objectives** This study evaluated data from 3 federally funded trials that focused on optimal medical therapy to determine if formalized attempts at risk factor control within clinical trials are effective in achieving guideline-driven treatment goals for diabetic patients with coronary artery disease (CAD).
- Background** Despite clear evidence of benefit for CAD secondary prevention, the level of risk factor control in clinical practice has been disappointing.
- Methods** We obtained data from the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) diabetes subgroup, (n = 766 of 2,287), the BARI 2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) trial (n = 2,368), and the FREEDOM (Comparison of Two Treatments for Multivessel Coronary Artery Disease in Individuals With Diabetes) trial (n = 1,900) to evaluate the proportion of patients achieving guideline-based, protocol-driven treatment targets for systolic blood pressure, low-density lipoprotein cholesterol, smoking cessation, and hemoglobin A1c. The primary outcome measure was the proportion of diabetic CAD patients meeting all 4 pre-specified targets at 1 year after enrollment.
- Results** The pooled data include 5,034 diabetic patients. The percentages of patients achieving the 1-year low-density lipoprotein cholesterol targets compared with baseline increased from 55% to 77% in COURAGE, from 59% to 75% in BARI 2D, and from 34% to 42% in FREEDOM. Although similar improved trends were seen for systolic blood pressure, glycemic control, and smoking cessation, only 18% of the COURAGE diabetes subgroup, 23% of BARI 2D patients, and 8% of FREEDOM patients met all 4 pre-specified treatment targets at 1 year of follow-up.
- Conclusions** A significant proportion of diabetic CAD patients fail to achieve pre-specified targets for 4 major modifiable cardiovascular risk factors in clinical trials. We conclude that fundamentally new thinking is needed to explore approaches to achieve optimal secondary prevention treatment goals. (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation; NCT00007657) (Bypass Angioplasty Revascularization Investigation 2 Diabetes [BARI 2D]; NCT00006305) (Comparison of Two Treatments for Multivessel Coronary Artery Disease in Individuals With Diabetes [FREEDOM]; NCT00086450) (J Am Coll Cardiol 2013;61:1607–15) © 2013 by the American College of Cardiology Foundation

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**Abbreviations
and Acronyms**

CAD	= coronary artery disease
DM	= diabetes mellitus
HbA1c	= hemoglobin A1c
LDL-C	= low-density lipoprotein cholesterol
OMT	= optimal medical therapy
PCI	= percutaneous coronary intervention
SBP	= systolic blood pressure

Coronary artery disease (CAD) is the leading cause of death and disability worldwide and is particularly prevalent among populations with diabetes and hypertension (1). Significant advances in revascularization techniques for the treatment of CAD have been accompanied by concomitant improvements in medical management over the past 2 decades. In general, contemporary optimal medical therapy (OMT) includes lifestyle interventions (heart-healthy diet, weight loss/maintenance, regular exercise, smoking cessation) and multifaceted pharmacotherapy aimed at controlling hyperlipidemia, hypertension, and diabetes mellitus (DM). Based on scientific evidence that the control of multiple cardiovascular risk factors reduces cardiovascular events (2), clinical practice guidelines have been established and disseminated broadly. These include guidelines from the Adult Treatment Panel III, the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, the American Diabetes Association, the American College of Cardiology, and the American Heart Association (3–6). Current Adult Treatment Panel III guidelines advocate a low-density lipoprotein cholesterol (LDL-C) goal of <100 mg/dl in patients with established CAD (3), with a more aggressive LDL-C goal of <70 mg/dl suggested for high-risk patients (7). In the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, the target blood pressure goal is <140/90 mm Hg in nondiabetic patients and <130/80 mm Hg in diabetic patients (4). Although the data for the reduction in cardiovascular events with glycemic control based on hemoglobin A1c (HbA1c) is controversial, the American Diabetes Association guidelines for diabetes management recommend a reasonable HbA1c goal of <7% (5,8). Finally, the updated American College of Cardiology/American Heart Association guidelines on secondary prevention and risk reduction in CAD

patients advocate active physician intervention and counseling for patients to quit smoking with an ultimate goal of complete tobacco cessation (6).

Thus, control of these 4 risk factors is associated with improved clinical outcomes and is the foundation of OMT for patients with CAD, regardless of whether patients undergo coronary revascularization (either percutaneous coronary intervention [PCI] or coronary artery bypass graft surgery) (2). Nevertheless, it has been documented that it is difficult to achieve risk factor control in routine clinical practice (9,10). Whether achievement of pre-specified treatment targets could be facilitated by a carefully designed, rigorous, and purposeful approach is unknown. For this reason, we hypothesized that protocol-driven risk factor reduction in major randomized trials may provide an effective platform for risk factor control. Accordingly, we examined the results in attaining secondary prevention targets among CAD patients with DM who were randomized from the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) (11,12), BARI 2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) (13), and FREEDOM (Comparison of Two Treatments for Multivessel Coronary Artery Disease in Individuals With Diabetes) (14) trials.

Methods

The principal investigators of 3 federally funded clinical trials involving coronary revascularization and OMT were approached and agreed to participate in a collaborative analysis to ascertain the degree to which pre-defined, trial-specific treatment targets for CAD risk factors were achieved between baseline and the 1-year follow-up. All 3 trials recognized the critical importance of risk factor control by establishing predetermined treatment targets for OMT. In general, OMT consisted of vascular disease-modifying interventions (aspirin, statins, inhibitors of the renin-angiotensin system, and thienopyridines as needed), therapeutic agents to control angina and myocardial ischemia (beta-blockers, calcium channel blockers, long-acting nitrates), and aggressive lifestyle interventions (nutrition counseling, weight loss, exercise, smoking cessation). The United States Veterans Affairs and Canadian Institutes of Health Research-funded COURAGE trial randomized 2,287 stable CAD patients from 1999 through 2004, comparing OMT with and without PCI; of note, 766 patients (34%) had DM. The nondiabetic patients in the COURAGE trial were the comparator group for the diabetic cohorts because the other trials enrolled only patients with diabetes. The National Heart, Lung, and Blood Institute-sponsored BARI 2D trial randomized 2,368 angiographically documented CAD patients with type II DM from 2001 through 2005 to either prompt revascularization (either PCI or coronary artery bypass graft, as decided by the patient's physician) with OMT, or OMT alone. Finally, in the National Heart, Lung, and Blood

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Table 1 Comparison of Secondary Prevention Risk Factor Targets by Trial

Target	COURAGE NDM	COURAGE DM	BARI 2D	FREEDOM
LDL-C (mg/dl)	100	100	100	70
SBP (mm Hg)	130	130	130	130
HbA1c (%)	—	7.0	7.0	7.0
Smoking (%)	0	0	0	0

Targets reported for this analysis using the pertinent contemporary guideline of the time.
 BARI 2D = Bypass Angioplasty Revascularization Investigation 2 Diabetes; COURAGE = Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation; DM = diabetes mellitus; FREEDOM = Comparison of Two Treatments for Multivessel Coronary Artery Disease in Individuals With Diabetes; HbA1c = hemoglobin A1c; LDL-C = low-density lipoprotein cholesterol; NDM = nondiabetes mellitus; SBP = systolic blood pressure.

Institute-sponsored FREEDOM trial, 1,900 diabetic patients with multivessel CAD were randomized from 2005 through 2010 to either PCI with drug-eluting stents or coronary artery bypass graft surgery. In this study, OMT was prescribed to the overall population, but the control of risk factors was relegated to community physicians. Overall, great effort was taken in all 3 trials to communicate with study centers and to develop strategies to enhance the achievement of risk factor goals. These protocols were described previously in detail (14–16). All 3 studies used feedback mechanisms and tracking programs to ensure that investigators were in constant communication with providers at the local sites to foster attainment of goals, especially when goals were not being achieved. The COURAGE and BARI 2D trials additionally used a case-managed approach with nurse practitioners or study coordinators organizing intensive, individualized protocol-driven care through multiple visits and close follow-up. All 3 trials were approved by the institutional review boards of all participating institutions.

Data were provided by the individual trial steering committees, which included baseline characteristics, medication use, and achievement of pre-specified treatment targets for LDL-C, systolic blood pressure (SBP), HbA1c, and smoking cessation. Medications ascertained included antiplatelet agents, lipid-lowering agents, and antihypertensive agents such as calcium-channel blockers, angiotensin II-converting enzyme inhibitors, angiotensin receptor blockers, and beta-blockers. Laboratory and clinical parameters analyzed included LDL-C, SBP, HbA1c (for DM patients), and percentage of smokers. Data were recorded from each trial in a uniform format, and data summaries from individual trials were checked against the associated publications for accuracy.

Statistical analysis. We compared diabetic patients among the COURAGE, BARI 2D, and FREEDOM trials and used the COURAGE nondiabetic cohort as a comparator group. Data were analyzed to calculate the proportion of patients meeting each pre-specified treatment target. Patients meeting all 4 targets were defined as nonsmokers who met the goal for LDL-C, SBP, and HbA1c (for DM patients) as defined by each respective trial (Table 1). All

available data at each time point (baseline and 1 year) were used in the analyses.

Results

The pooled data for the population under study comprised 5,034 diabetic patients with CAD. Despite the different study designs, the baseline characteristics of the enrolled patients generally were similar across the trials (Table 2). In all 3 trials, use of proven secondary prevention therapies increased between baseline and the 1-year follow-up (Table 3). Table 4 demonstrates that the mean values of attained risk factor goals across the trial populations at 1 year of follow-up decreased to levels within, or close to, targets as pre-specified by each respective trial.

Low-density lipoprotein cholesterol. In the COURAGE nondiabetic group, 46% of patients achieved the LDL-C goal of <100 mg/dl at baseline (Table 5) (Fig. 1). At 1 year, this improved to 74%. Similarly in the COURAGE trial DM patients, 55% met the LDL-C target at baseline, which improved to 77% at 1 year. The percentage of patients meeting LDL-C goals increased similarly in the BARI 2D trial, improving from 59% to 75% at 1 year. Given the evolution of guideline standards, a more stringent target of <70 mg/dl was used in the FREEDOM trial. At 1 year, only 42% of patients met this goal, improving from a baseline of 34%. However, for comparative purposes across all studies, we note that 62% of FREEDOM patients had an LDL-C of <100 mg/dl at baseline and 75% achieved the LDL-C goal of <100 mg/dl at 1 year. Thus, for all 3 trials, the percentage of diabetic patients with CAD who attained an LDL-C of <100 mg/dl at 1 year ranged from 75% to 77%.

Systolic blood pressure. All 3 trials used an SBP target of <130 mm Hg in both patients with and without DM. Nondiabetic patients in the COURAGE trial fared better, improving from 46% to 60% meeting the target after 1 year (Table 5) (Fig. 2). Conversely, the SBP target in diabetic patients in the COURAGE trial improved from a baseline of 37% to only 49%, whereas in the BARI 2D trial, with exclusively diabetic patients, the percentage of patients who achieved their target SBP goal increased from 49% to 56%. In the FREEDOM trial, the percentage of patients who achieved the SBP goal decreased slightly from 40% to 38% at 1 year. In all 3 studies, more than 80% of patients were taking a beta-blocker at 1 year, with most patients taking at least 1 antihypertensive medication. As was found with LDL-C, mean values for blood pressure targets seemed favorable, but one-quarter to two-thirds of subjects had SBP values higher than the trial-specified target at 1 year.

Glycemic control. Approximately one-half of diabetic patients in all 3 trials did not achieve an HbA1c level of <7% at 1 year (Table 5) (Fig. 3). There was little evidence of improved glycemic control in the diabetic group in the COURAGE trial at 1 year, decreasing from 50% to 48% of those achieving the target HbA1c. In the BARI 2D trial, the 1-year glycemic control rate was 51%, a substantial

Table 2 Baseline Patient Characteristics of the 3 Trials

	COURAGE NDM (n = 1,482)	COURAGE DM (n = 766)	BARI 2D (n = 2,368)	FREEDOM (n = 1,900)
Mean age (yrs)	62.0	62.4	62.4	63.1
Female (%)	15	14	30	29
Ethnic minority* (%)	11	21	34	49
Angina (%)	88	88	82	86
Prior MI (%)	40	37	32	26
Prior PCI (%)	14	18	20	1.2
Prior CABG (%)	10	13	6	0
Heart failure history (%)	3	8	7	27
Stroke/TIA (%)	7	10	10	3
PAD (%)	6	11	24	11

*Non-Caucasian white.

CABG = coronary artery bypass graft; MI = myocardial infarction; PAD = peripheral artery disease; PCI = percutaneous coronary intervention; TIA = transient ischemic attack. Other abbreviations as in Table 1.

increase from the 40% of patients meeting the HbA1c target at baseline. In the FREEDOM trial, 45% of diabetic CAD patients met the HbA1c goal at 1 year, increasing from 37% at baseline.

Smoking cessation. In the COURAGE trial, nondiabetic patients who were nonsmokers increased from 69% at baseline to 77% at 1 year. Among COURAGE DM patients, the rate of nonsmokers improved from 76% at baseline to 86% at 1 year. In the BARI 2D trial, 88% met the target at baseline and 90% met the target at 1 year, whereas in the FREEDOM trial, 84% were not smoking at baseline, which increased to 94% at 1 year.

Proportion of CAD patients with DM achieving all 4 treatment targets. Given the inherent difficulty in controlling individual risk factors, it is perhaps not surprising that no trial achieved more than 25% of their diabetic patients who were able to achieve the trial-specified composite targets for all 4 major risk factor targets (LDL-C, SBP, HbA1c, and smoking cessation) (Table 5) (Fig. 4). In the COURAGE nondiabetic group, 46% achieved all 3 targets (no HbA1c target for nondiabetic patients) at 1 year, compared with 16% at baseline. By contrast, only 18% of the diabetic subgroup achieved all 4 treatment targets at 1 year compared with 7% at baseline. In the BARI 2D trial, 23% of patients reached all 4 targets at 1 year, compared with 14% at baseline. With the more stringent LDL-C target of <70 mg/dl in the FREEDOM trial, only 8% of

patients met all 4 major goals at 1 year, compared with 4% at baseline.

Discussion

The principal finding of this collaborative analysis of data from 5,034 diabetic patients with CAD enrolled in the COURAGE, BARI 2D, and FREEDOM trials is that the percentage of patients who simultaneously achieved pre-specified treatment goals for LDL-C, SBP, HbA1c, and smoking cessation 1 year after randomization was low, ranging from 8% to 23%. This finding is disappointing in the context of randomized clinical trials, in which highly competent teams of multidisciplinary healthcare providers with specialized training interacted with patients in a clinical trial setting that created a clinical care environment where risk factor management was facilitated. The reasons for the limited success in achieving risk factor control for all 4 risk factors in diabetic patients with CAD may be related to complex interactions of the patients' disease burden, their lifestyle behavior, the medical team, and their underlying socioeconomic environment.

When compared with the proportion of patients having all 4 risk factors under control, the percentage of patients meeting individual targets was higher. For instance, LDL-C of <100 mg/dl was observed in approximately 75% of diabetic patients, and the SBP goal of <130/80 mm Hg

Table 3 Proportion Prescribed Each Medication in the 3 Trials at 1 Year

	COURAGE NDM		COURAGE DM		BARI 2D		FREEDOM	
	Baseline (n = 1,236)	1 Year (n = 1,366)	Baseline (n = 589)	1 Year (n = 674)	Baseline (n = 2,368)	1 Year (n = 2,142)	Baseline (n = 1,900)	1 Year
Lipid lowering (%)	70	97	71	96	79	98	86	94
Statins (%)	67	95	67	93	75	94	82	90
ACEI/ARB (%)	46	66	65	84	77	90	78	80
Beta-blocker (%)	72	85	70	90	73	86	75	82
CCB (%)	29	43	33	47	10	9	32	23
Aspirin (%)	87	96	88	94	88	92	91	96

ACEI/ARB = angiotensin II-converting enzyme inhibitor/angiotensin II receptor blocker; CCB = calcium channel blocker; other abbreviations as in Table 1.

Table 4 Mean Values for Cardiovascular Risk Factors at Baseline and 1 Year in the 3 Trials

Risk Factor	COURAGE NDM		COURAGE DM		BARI 2D		FREEDOM	
	Baseline (n = 1,482)	1 Year (n = 1,366)	Baseline (n = 766)	1 Year (n = 672)	Baseline (n = 2,368)	1 Year (n = 2,142)	Baseline (n = 1,900)	1 Year
LDL-C (mg/dl)	107 ± 34	86 ± 27	101 ± 27	83 ± 29	96 ± 33	86 ± 28	93 ± 36	83 ± 34
SBP (mm Hg)	131 ± 19	125 ± 17	135 ± 17	130 ± 19	132 ± 20	128 ± 16	134 ± 20	134 ± 19
HbA1c (%)	5.5 ± 0.6	—	7.2 ± 1.6	7.4 ± 1.6	7.7 ± 1.6	7.2 ± 1.4	7.8 ± 1.7	7.4 ± 1.6
Smoking (%)	31 (29-33)	23 (21-26)	24 (21-27)	14 (11-17)	12 (11-14)	10 (9-11)	16 (14-17)	6 (5-8)

Values are mean ± SD or % (95% confidence interval).
 Abbreviations as in Table 1.

ranged from 38% to 56% at 1 year. The achievement of individual goals in this study of high-risk patients was better than has been reported for the general diabetic population (17-19).

Numerous factors likely contributed to the limited success in achieving composite risk-factor goals in these 3 trials. Among the potential contributors is a lack of physician compliance with evidence-based American College of Cardiology/American Heart Association management guidelines (6,20), although the extent to which this adversely impacted risk factor control in these studies was not examined specifically. However, investigators in the 3 trials communicated frequently with the community physicians caring for the patients with newsletters, educational materials, and other communications to increase the likelihood that appropriate medications at appropriate doses would be prescribed to achieve secondary prevention goals.

Another difficulty in achieving multiple risk-factor goals is the inherent challenge of medication regimen adherence by patients. In routine practice, medication prescriptions often are not filled or continued long-term. Barriers may include cost, the burden of taking multiple medications, drug-drug interactions, and side effects (21). The complex problem of limited patient adherence is underscored by the heterogeneity of compliance improvement when cost is removed as a factor. A recent trial indicated that patient adherence rates after a myocardial infarction improved only marginally if the medications were provided free of charge (22).

Even if medications are prescribed and prescriptions are filled, patient nonadherence remains a problem. Among factors that may modulate patient adherence are

advanced age, comorbid conditions, complexity of treatment regimen, health beliefs, healthcare setting, socioeconomic status, social support, and psychological state (21,23). These and other factors may result in patients deciding on their own to avoid adhering to risk factor modification regimens.

Among patients with chronic disease states, such as diabetic patients with CAD, more than 50% show poor adherence to treatment and fewer than 30% follow the recommended lifestyle modifications (24). Underscoring the importance of adherence to patient outcomes, several studies have shown that the continuous use of medications after hospital discharge for acute coronary syndromes was associated independently and strongly with lower mortality (25-27). However, such data in stable CAD patients largely are lacking.

The limited success of risk factor control, even when vigorously attempted, suggests that current risk-factor control approaches have significant limitations that need to be overcome with new paradigms. For example, one novel approach to improving adherence based on simplifying medical regimen complexity is to combine medications indicated for secondary prevention into one pill. This concept of a so-called polypill was proposed first by Wald and Law (28) and consisted of 6 agents (3 blood pressure-lowering agents from different classes plus aspirin, a statin, and folic acid). Since then, various different formulations of polypills have been introduced and are being investigated for secondary prevention (29,30). Although large-scale randomized trials have not yet been completed to evaluate the advantages of combining guideline-based agents for secondary prevention, a study of patients with CAD, diabetes, or

Table 5 Proportion of Patients Meeting Targets in the 3 Trials Over 1 Year

Risk Factor	COURAGE NDM		COURAGE DM		BARI 2D		FREEDOM	
	Baseline (n = 1,478)	1 Year (n = 1,367)	Baseline (n = 762)	1 Year (n = 764)	Baseline (n = 2,368)	1 Year (n = 2,142)	Baseline (n = 1,900)	1 Year
LDL-C (%)	46	74	55	77	59	75	34	42
SBP (%)	46	60	37	49	49	56	40	38
HbA1c (%)	—	—	50	48	40	51	37	45
Nonsmoking (%)	69	77	76	86	88	90	84	94
Met All 4 goals	16	46	7	18	14	23	4	8

Targets were defined as follows (see Table 1): LDL-C: <100 mg/dl (except for FREEDOM, with LDL-C <70 mg/dl), SBP: <130 mm Hg, HbA1c: <7.0, and nonsmoking.
 Abbreviations as in Table 1.

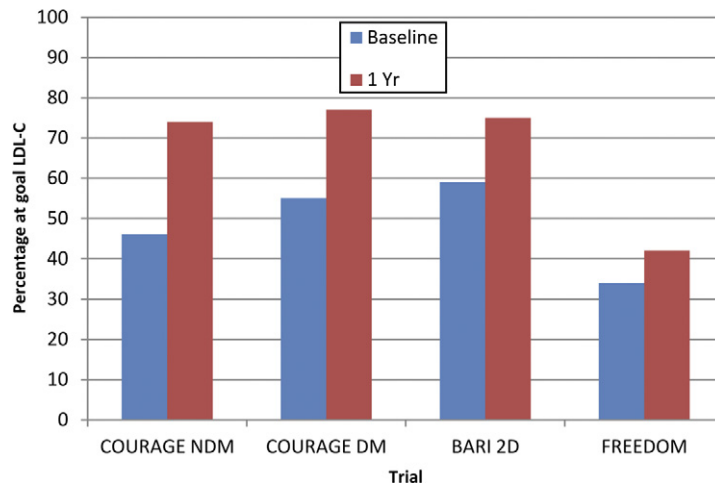


Figure 1 Percentage of Patients Achieving Target LDL-C Levels Among the 3 Trials From Baseline to 1 Year of Follow-Up

The COURAGE trial was divided into diabetes (DM) and nondiabetes (NDM) cohorts. Goal low-density lipoprotein cholesterol (LDL-C) was defined as <100 mg/dl for COURAGE and BARI 2D and <70 mg/dl for FREEDOM.

both showed that the use of a simplified regimen of fixed doses of statin and angiotensin II-converting enzyme inhibitors or angiotensin receptor blockers was feasible and decreased the risk of hospitalizations for ischemic heart disease or stroke within 1 year (31). Further large-scale studies evaluating the impact of a polypill intervention on the attainment of cardiovascular risk factor targets in high-risk patients are warranted.

Study limitations. Although this study highlights the limited degree to which complete risk factor control was achieved in these trials, there are several limitations. It is conceivable that risk factor values for patients at 1 year were near the goal, but had not completely reached the target.

Because we used an absolute cutoff for the measure of control, such borderline patients would not have been captured by this analysis. This is one plausible explanation for why the mean values of risk factors in all 3 trials seemed to be more favorable as compared with the proportion of patients meeting the targets. Although we acknowledge that non-high-density lipoprotein cholesterol may be a better metric for risk in diabetic patients as compared with LDL-C, we used only targets that were pre-specified by trial design. Finally, there has been recent debate over the goal of hypertension control in the elderly age group (older than 80 years) (32). In our analysis, we used targets and guidelines that were contemporary to the era of the respec-

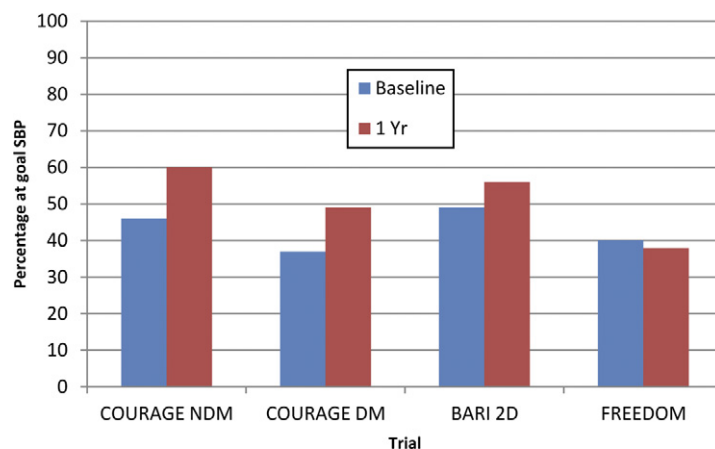


Figure 2 Percentage of Patients Achieving Goal Values for SBP Among the 3 Trials From Baseline to 1 Year of Follow-Up

The COURAGE trial was divided into DM and NDM cohorts. Goal systolic blood pressure (SBP) was defined as <130 mm Hg for the COURAGE, BARI 2D, and FREEDOM trials. Abbreviations as in Figure 1.

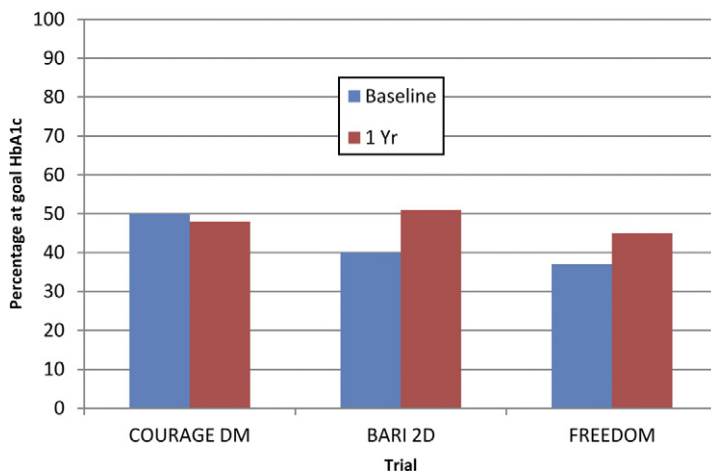


Figure 3 Percentage of Patients Achieving Goal Values for Hemoglobin A1c Among the 3 Trials From Baseline to 1 Year of Follow-Up

For the COURAGE trial, only the DM subgroup was analyzed. Target hemoglobin A1c (HbA1c) was defined as <7.0% for the COURAGE, BARI 2D, and FREEDOM trials. Abbreviations as in Figure 1.

tive trials. The goals were set before the release of this newer evidence.

The known clinical benefit of risk factor control juxtaposed with the demonstrated inability to achieve satisfactory control rates for multiple cardiac risk factors in the ideal setting of the randomized clinical trial raises the possibility that a combination of formidable barriers exist. Individually, these barriers do not seem to be insurmountable, but in the aggregate, they create fundamental limitations on what

optimal risk factor control efforts can achieve. Would providing more broad-based educational initiatives facilitate healthcare team adherence to existing clinical practice guidelines? Would greater attention to each step in the chain of events that control risk factors (healthcare team efforts, patient adherence) improve the results? These 3 trials used a multidisciplinary healthcare team approach, including advanced nurse practitioners, registered dietitians, and diabetic educators (to varying degrees), but largely were

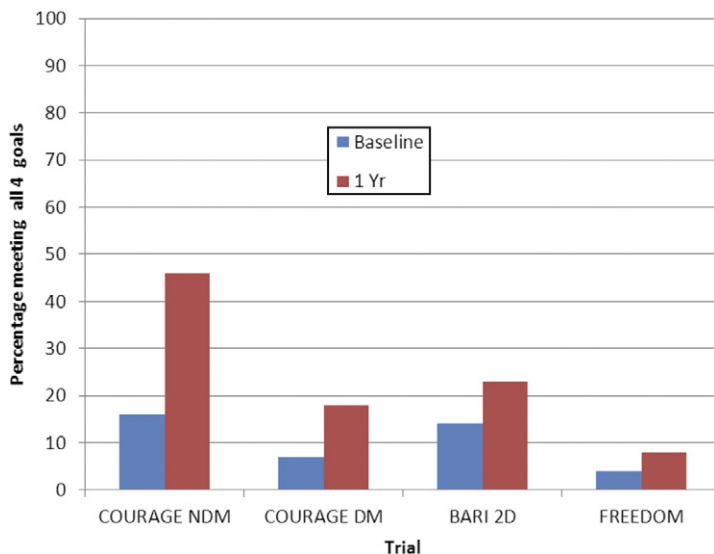


Figure 4 Percentage of Patients Meeting All 4 Targets (LDL-C, SBP, HbA1c, and Smoking Cessation) Among the 3 Trials From Baseline to 1 Year of Follow-Up

The COURAGE trial was divided into DM and NDM cohorts. Targets were pre-specified by trial and included 4 items: LDL-C, SBP, HbA1c, and smoking cessation. Abbreviations as in Figure 1.

ineffective in achieving and maintaining a high level of risk-factor control.

Conclusions

In 3 major randomized clinical trials of revascularization strategies where secondary prevention attempts were undertaken to optimize multiple treatment targets in CAD patients with diabetes, individual risk factor control was improved compared with baseline, but the proportion of patients achieving treatment goals for 4 major cardiac risk factors (LDL-C, SBP, HbA1c, and smoking cessation) was limited. These data suggest the possibility of a ceiling effect on what can be achieved therapeutically in real-world clinical practice with respect to controlling multiple cardiac risk factors simultaneously. There is a compelling imperative to explore and define new management paradigms and novel treatment approaches to optimize risk-factor control for secondary prevention.

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