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ORIGINAL RESEARCH

Sex Differences in Revascularization, Treatment Goals, and Outcomes of Patients With Chronic Coronary Disease: Insights From the ISCHEMIA Trial

Harmony R. Reynolds, MD; Derek D. Cyr, PhD, MS; C. Noel Bairey Merz, MD; Leslee J. Shaw, PhD; Bernard R. Chaitman, MD; William E. Boden, MD; Karen P. Alexander, MD; Yves D. Rosenberg, MD, MPH; Sripal Bangalore, MD, MHA; Gregg W. Stone, MD; Claes Held, MD, PhD; John Spertus, MD, MPH; Kaatje Goetschalckx, MD; Olga Bockeria, MD, PhD; Jonathan D. Newman, MD, MPH; Jeffrey S. Berger, MD, MS; Ahmed Elghamaz, MD; Renato D. Lopes, MD, PhD; James K. Min, MD; Daniel S. Berman, MD; Michael H. Picard, MD; Raymond Y. Kwong, MD, MPH; Robert A. Harrington, MD; Boban Thomas, MD; Sean M. O'Brien, PhD; David J. Maron, MD; Judith S. Hochman, MD; on behalf of the ISCHEMIA Research Group*

BACKGROUND: Women with chronic coronary disease are generally older than men and have more comorbidities but less atherosclerosis. We explored sex differences in revascularization, guideline-directed medical therapy, and outcomes among patients with chronic coronary disease with ischemia on stress testing, with and without invasive management.

METHODS AND RESULTS: The ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) trial randomized patients with moderate or severe ischemia to invasive management with angiography, revascularization, and guideline-directed medical therapy, or initial conservative management with guideline-directed medical therapy alone. We evaluated the primary outcome (cardiovascular death, myocardial infarction, or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest) and other end points, by sex, in 1168 (22.6%) women and 4011 (77.4%) men. Invasive group catheterization rates were similar, with less revascularization among women (73.4% of invasive-assigned women revascularized versus 81.2% of invasive-assigned men; $P<0.001$). Women had less coronary artery disease: multivessel in 60.0% of invasive-assigned women and 74.8% of invasive-assigned men, and no ≥50% stenosis in 12.3% versus 4.5% ($P<0.001$). In the conservative group, 4-year catheterization rates were 26.3% of women versus 25.6% of men ($P=0.72$). Guideline-directed medical therapy use was lower among women with fewer risk factor goals attained. There were no sex differences in the primary outcome (adjusted hazard ratio [HR] for women versus men, 0.93 [95% CI, 0.77–1.13]; $P=0.47$) or the major secondary outcome of cardiovascular death/myocardial infarction (adjusted HR, 0.93 [95% CI, 0.76–1.14]; $P=0.49$), with no significant sex-by-treatment-group interactions.

CONCLUSIONS: Women had less extensive coronary artery disease and, therefore, lower revascularization rates in the invasive group. Despite lower risk factor goal attainment, women with chronic coronary disease experienced similar risk-adjusted outcomes to men in the ISCHEMIA trial.

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Key Words: coronary artery disease ■ ischemic heart disease ■ sex differences ■ women's health

Correspondence to: Harmony R. Reynolds, MD, NYU Cardiovascular Clinical Research Center, Leon H. Charney Division of Cardiology, Department of Medicine, NYU Grossman School of Medicine, 530 First Ave, SKI-9R, New York, NY 10016. Email: harmony.reynolds@nyulangone.org

*A complete list of the ISCHEMIA Research Group members can be found in the Appendix at the end of the article.

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CLINICAL PERSPECTIVE

What Is New?

- Cardiac catheterization rates were similar by sex in both the routine invasive management strategy group and the conservative management strategy group, but women had lower likelihood of obstructive coronary artery disease at angiography, and therefore underwent revascularization less often than men in both groups, despite a requirement for moderate or severe ischemia on stress testing.
- Use of guideline-directed medical therapy was lower among women than men in the trial, with fewer treatment goals achieved, despite protocolized trial guidance on medical therapy.
- Rates of the primary and secondary clinical outcomes were not different by sex.

What Are the Clinical Implications?

- The similar clinical outcomes for men and women randomized in the ISCHEMIA (International Study of Comparative Health Effectiveness with Medical Invasive Approaches) trial represent the net effects of sex differences that reflect opposing risks: women were older than men and had higher rates of hypertension and diabetes with poorer risk factor control throughout follow-up, but had less extensive anatomic coronary artery disease and ischemia on imaging.
- Additional efforts are needed to achieve equity in risk factor control for women and men with chronic coronary disease.

Nonstandard Abbreviations and Acronyms

CCD	chronic coronary disease
GDMT	guideline-directed medical therapy

In patients with chronic coronary disease (CCD), the prevalence of obstructive coronary artery disease (CAD) is lower in women than in men, whereas, conversely, there is a higher prevalence of ischemia with no obstructive coronary arteries in women.[1,2] Women, in general, often present at older ages and with more clinical comorbidities than men.[3,4] However, unlike patients presenting with acute coronary syndromes, women with CCD have not been shown to be at higher risk of adverse cardiovascular outcomes compared with men in previously published clinical trials and registries.[5–12]

Unique among studies of patients with CCD, the ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) trial randomized participants before cardiac catheterization to an initial invasive or conservative management strategy. Site-assessed moderate or severe ischemia at baseline was a prerequisite for trial inclusion, resulting in a high prevalence of severe multivessel CAD.[13] Enrolled participants with adequate renal function had prerandomization coronary computed tomography angiography (CCTA) to confirm the presence of at least 50% stenosis in a coronary artery and to exclude patients with significant left main CAD. Consequently, this process excluded more women than men because of the higher prevalence of ischemia with no obstructive coronary arteries, and even among those randomized, women had less severe and extensive anatomic CAD than men.[14] Prior studies have demonstrated that, compared with men, women with CCD have lower rates of revascularization, particularly surgical revascularization, and may have poorer outcomes after revascularization.[15–18] However, the extent to which lower rates of revascularization among women may relate to sex differences in severity of ischemia remains unknown. Lower use of guideline-directed medical therapy (GDMT) among women may also affect outcomes.[19,20] GDMT recommendations are identical for patients with CCD of both sexes, yet gaps in care remain. The extent to which protocolized guidance within a clinical trial structure may narrow these gaps requires further investigation.

Women had more severe angina at randomization in the ISCHEMIA trial, independent of other clinical variables.[14] This greater angina burden is consistent with observational studies and has the potential to influence the likelihood of symptom-driven cardiac catheterization and revascularization during follow-up.[21,22] Women with acute coronary syndrome exhibit lower troponin values than men, and sex-specific high-sensitivity troponin assays improve the diagnosis of myocardial infarction (MI); thus, sex has the potential to influence reporting and adjudication of acute coronary syndrome events occurring during clinical trial follow-up.[23,24] Thus, the aim of this analysis was to compare outcomes and medical therapy use between women and men with CCD randomized in the ISCHEMIA trial to help inform the future management of women with CCD.

METHODS

Deidentified ISCHEMIA trial data will be shared with researchers through the National Heart, Lung, and Blood Institute BioLINCC repository (https://biolincc.nhlbi.nih.gov/). The ISCHEMIA trial design has been published.[25] In brief, patients with site-assessed moderate or severe ischemia based on stress testing were randomized to an initial invasive management strategy

or an initial conservative management strategy. CCTA was performed before randomization to ensure that randomized participants had significant epicardial coronary stenosis but not left main disease but was not required if the estimated glomerular filtration rate was <60 mL/min per 1.73 m^2 or the coronary anatomy was known to meet entry criteria based on recent imaging. Major exclusion criteria were acute coronary syndrome within 2 months before randomization, left ventricular ejection fraction <35%, unacceptable angina severity despite maximal medical therapy, estimated glomerular filtration rate <30 mL/min per 1.73 m^2, heart failure hospitalization within the past 6 months, and New York Heart Association class III to IV heart failure. The study was approved by the NYU School of Medicine Institutional Review Board and by the review board of each participating site. All patients provided informed consent to participate in the ISCHEMIA trial.

All participants were to receive GDMT, and sites were provided algorithms to guide pharmacologic treatment to targets of low-density lipoprotein cholesterol (LDL-C) <70 mg/dL and systolic blood pressure (SBP) <140 mm Hg. The SBP goal was later lowered to <130 mm Hg, but we used the original goal in this analysis. Participants with diabetes were to be treated to a goal hemoglobin A1c of <8%, but this was not considered a primary goal, and a treatment algorithm was not provided. Lifestyle interventions were applied in a protocolized manner toward goals of lower saturated fat in the diet, increased activity level, normal body mass index, and nonsmoking. Medication-taking behavior was assessed by self-report at the time of randomization, using a modified 4-item Morisky-Green-Levine Adherence Scale, allowing participants to be classified as adherent or nonadherent.

Participants randomized to the invasive strategy were to undergo cardiac catheterization with revascularization of all ischemic territories based on stress test results, diagnostic angiography, or measurement of fractional flow reserve. An algorithm was used to guide complete revascularization, and a Heart Team approach was used by sites to determine suitability of patients with complex anatomy for percutaneous coronary intervention or coronary artery bypass grafting as the method of revascularization.

An angiographic core laboratory reviewed coronary angiograms from patients enrolled in the invasive group to determine the severity of stenosis, extent of disease, and completeness of revascularization. Extent and severity of CAD were quantified using the Duke Jeopardy Score and the Synergy between Percutaneous Coronary Intervention with TAXus and Cardiac Surgery score, as well as the number of vessels with ≥50% or ≥70% stenosis.[26,27]

The primary end point was a composite of cardiovascular death, nonfatal MI, or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest. The major secondary clinical outcome was the composite of cardiovascular death or nonfatal MI. Additional secondary outcomes were each component of the primary outcome, all-cause mortality, and stroke. Clinical outcomes were reported by sites or identified in the electronic data capture system and were adjudicated by an independent clinical events committee blinded to treatment strategy allocation. Health status outcomes represented a major secondary outcome and will be reported in relation to sex separately. The use of, and reasons for, cardiac catheterization and revascularization were collected in both treatment strategy groups during follow-up. MI was defined according to trial criteria and was categorized according to type.[25,28] Procedural MI was defined as type 4a or 5. To increase ascertainment of MI and unstable angina, sites were required to report all emergency department visits and hospitalizations and to report whether cardiac markers were collected, the values, and the discharge diagnoses associated with these visits. All end point events were adjudicated by an independent clinical events classification committee whose members were blinded to the study treatment assignment.

Statistical Analysis

Outcomes were assessed according to biological sex, which was known for all randomized participants and assessed by self-report. We did not collect sex. For simplicity of language in this report, we refer to females as women and males as men. Baseline characteristics are presented separately for women and men within each treatment group. Categorical variables are presented as counts (percentages), and differences between women and men were assessed using the χ^2 test or Fisher exact test, as appropriate. Continuous variables are presented as the number of nonmissing values and median (quartile 1–quartile 3), and differences between women and men were compared using the Wilcoxon rank-sum test or Student *t*-test, as appropriate. Imputation was not performed for descriptive tables; missing data are excluded from all denominators. The α level was set at 0.05.

To distinguish the timing of clinical events, cumulative event rates and 95% CIs are estimated as a function of follow-up time in women and men with use of the Kaplan-Meier method[29] for events that are not subject to competing risks (eg, all-cause mortality) and by a nonparametric cumulative incidence function estimator[30] for events that are subject to competing risks (eg, cardiovascular death or MI, where death from noncardiovascular causes is treated as a competing event). The cumulative incidence function estimators for competing risks data are identical to the Kaplan-Meier estimate when applied to end points

that are not subject to competing risks. The associated *P* values from the Gray test[31] or log-rank test are also presented. To characterize the association of sex on clinical outcomes, the number of confirmed first events and hazard ratios (HRs; comparing women versus men), 95% CIs, and *P* values from unadjusted and adjusted Cox regression models are reported. As was specified in the ISCHEMIA main trial final analysis, adjustment covariates include age at randomization, estimated glomerular filtration rate, ejection fraction, diabetes, and randomized treatment strategy group.[32] Each "adjusted" model also assessed sex-by-age, sex-by-treatment, sex-by-degree of ischemia, and sex-by-diabetes interactions. To maximize the amount of information each covariate provides to the covariate-adjusted analysis, multiple imputation, using the same approach as was used in the main trial, was used to impute missing covariate data (Data S1).[28] To account for nonlinear relationships, continuous variables were modeled as restricted cubic splines with knots at the 10th, 50th, and 90th percentiles of each variable's empirical distribution. Unadjusted cumulative incidence

Table 1. Use of Catheterization and Revascularization in Participants Randomized to the Invasive Strategy Group by Sex

Characteristic	Women (N=606)	Men (N=1982)	*P* value
Participants with at least 1 catheterization during follow-up	570/606 (94.1)	1859/1982 (93.8)	0.81
Time from randomization to first catheterization, d	18 (9–31)	20 (10–31)	0.28
Fractional flow reserve testing used	119/568 (21.0)	400/1854 (21.6)	0.75
Participants with at least 1 revascularization during follow-up	445/606 (73.4)	1609/1982 (81.2)	<0.001
Time from randomization to first revascularization, d	24 (11–45)	27 (14–52)	0.02
First revascularization was PCI	352/445 (79.1)	1172/1609 (72.8)	0.008
Time from randomization to first PCI, d	22 (9–41)	22 (12–41)	0.24
Drug-eluting stent placed	319/352 (90.6)	1069/1171 (91.3)	0.70
First revascularization was CABG	93/445 (20.9)	437/1609 (27.2)	0.008
Time from randomization to first CABG, d	37 (22–76)	45 (25–89)	0.50
IMA graft placed during CABG	84/93 (90.3)	402/436 (92.2)	0.55
Participants with at least 1 catheterization or revascularization during follow-up	582/606 (96.0)	1893/1982 (95.5)	0.58
Catheterization or revascularization performed within 90 d of randomization	561/606 (92.6)	1822/1982 (91.9)	0.61
With 1-vessel CAD	86/96 (89.6%)	242/264 (91.7%)	5.54
With 2-vessel CAD	88/93 (94.6%)	316/341 (92.7%)	0.51
With 3 -vessel CAD	96/102 (94.1%)	546/592 (92.2%)	0.50
Site-reported reason for no catheterization performed by 6-wk visit			0.49
Patient preference	27/45 (60.0)	91/160 (56.9)	
Physician preference	2/45 (4.4)	5/160 (3.1)	
Intercurrent illness	4/45 (8.9)	10/160 (6.3)	
Participant died	1/45 (2.2)	0/160 (0.0)	
Other	6/45 (13.3)	29/160 (18.1)	
Missing or unknown	5/45 (11.1)	22/160 (13.8)	
Intended management strategy after first diagnostic catheterization in participants with a catheterization	137	284	
Medical therapy only	127/137 (92.7)	244/284 (85.9)	0.02
Reason for medical therapy			0.002
No obstructive CAD	91/127 (71.7)	130/244 (53.3)	
Anatomy not suitable for any mode of revascularization	23/127 (18.1)	88/244 (36.1)	
Patient preference	8/127 (6.3)	20/244 (8.2)	
Other	5/127 (3.9)	6/244 (2.5)	
PCI/CABG/hybrid	9/137 (6.6)	40/284 (14.1)	
Undecided	0/137 (0.0)	0/284 (0.0)	
Unknown	1/137 (0.7)	0/284 (0.0)	
Missing	0/137 (0.0)	0/284 (0.0)	

Data are given as number/total (percentage) or median (quartile 1–quartile 3). CABG indicates coronary artery bypass grafting; CAD, coronary artery disease; IMA, internal mammary artery; and PCI, percutaneous coronary intervention.

function estimates (accounting for the competing risk of death) of catheterization or revascularization were summarized over several time points by sex. Estimates were computed separately for participants randomized to the 2 treatment strategy groups. Descriptive statistics on the use of catheterization and revascularization in both treatment groups were summarized and compared by sex using the same previously stated methods.

The distribution of total emergency department admissions was tabulated among women and men and compared using a *t*-test or Wilcoxon rank-sum test, as appropriate. For medical therapy analysis, the proportion of participants meeting each goal at the end of the study was summarized, with end of study defined as the latest visit (at least 12 months after randomization) at which the goal was evaluable. If the latest visit where the goal is evaluable was <12 months after randomization, then the individual goal was considered to be missing. Note that the SBP goal of <140 mm Hg was used here, although by the end of the trial, sites were asked to use an SBP treatment goal of <130 mm Hg.

RESULTS

Patient Population

A total of 1168 (22.6%) women and 4011 (77.4%) men were randomized. As previously reported, hypertension and diabetes were more common among women, and women were slightly older than men.[14] Women were less likely to smoke and to have history of MI or prior coronary revascularization. Women were more likely to have been enrolled after stress imaging rather than exercise tolerance testing than men, and women had less severe ischemia on imaging than men. Fewer women underwent CCTA than men (67.4% versus 70.0%; *P*=0.02).[14] Randomized women also had less extensive and severe anatomic CAD on study CCTA than randomized men, and women had overall lower degrees of ischemia, and slightly higher left ventricular ejection fraction.[14] Baseline characteristics were well balanced between treatment strategy arms within each sex (Table S1).

Protocol-Assigned Invasive Procedures by Sex

Although there was no difference in the proportion of women and men randomized to the invasive strategy who underwent cardiac catheterization or in the timing of catheterization after randomization, women were less likely to undergo revascularization (73.4% of invasive-assigned women received revascularization versus 81.2% of invasive-assigned men; *P*<0.001) (Table 1; Figure 1A). Women had less severe CAD at invasive angiography than men, with more nonobstructive disease (12.3% versus 4.5% with no stenosis ≥50%; *P*<0.001) and less 3-vessel CAD (29.8% versus 42.7%; *P*<0.001) (Table 2). Within the subgroup of invasive-assigned patients who underwent CCTA, women still had higher likelihood of nonobstructive CAD on invasive angiography (10.2% versus 3.9%; *P*<0.001). Consistent with this, the most common reason that revascularization was not performed was the absence of obstructive CAD, which was the reason in 71.7% of women not revascularized versus 53.3% of men. The likelihood of revascularization did not differ by sex in analysis stratified by the number of diseased vessels at coronary angiography (Table 2). In the invasive strategy group, the first revascularization was more likely to be percutaneous coronary intervention in women compared with men (79.1% versus 72.8%; *P*=0.008). Within the subset of patients with 3- or 2-vessel CAD, including

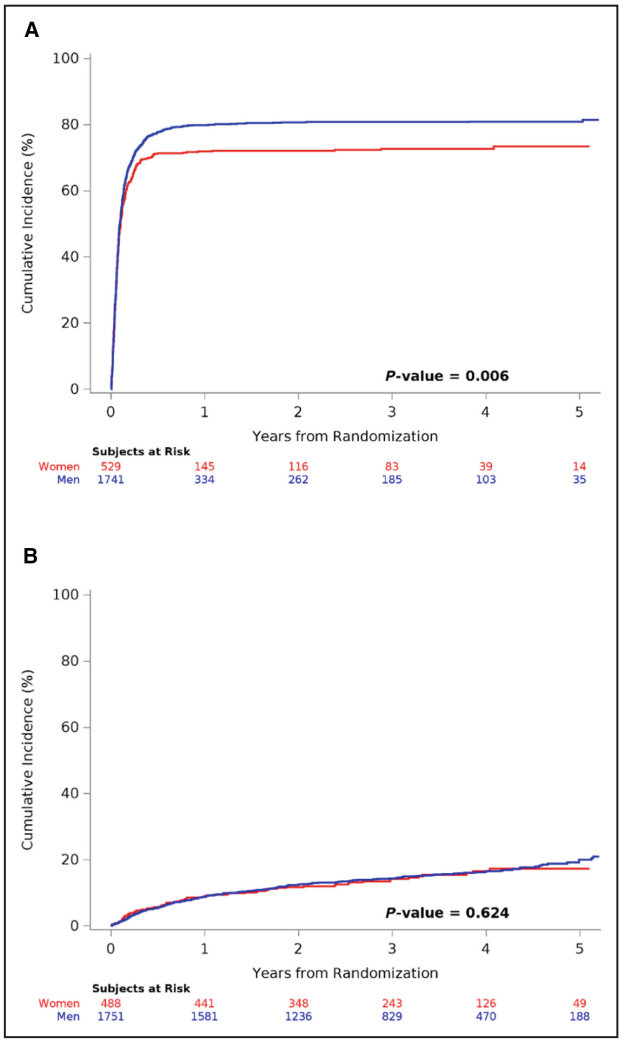

Figure 1. Unadjusted cumulative incidence plot of revascularization by sex, excluding revascularization for a suspected primary end point event.
A, Invasive strategy. **B**, Conservative strategy. Note that revascularization prompted by a suspected end point event is not included.

Table 2. Invasive Angiographic Findings in Participants Randomized to the Invasive Strategy Group by Sex

Characteristic	Women (N=578)	Men (N=1895)	*P* value
Any obstructive disease ≥50% stenosis			
Overall	504/573 (88.0)	1795/1877 (95.6)	<0.001
After CCTA performed	362/403 (89.8)	1425/1483 (96.1)	<0.001
No. of native vessels with ≥50% stenosis			<0.001
0 Vessels	69/560 (12.3)	82/1811 (4.5)	
Revascularization done	5/69 (7.2)	3/82 (3.7)	0.47
1 Vessel	155/560 (27.7)	374/1811 (20.7)	
Revascularization done	124/155 (80.0)	314/374 (84.0)	0.27
2 Vessels	169/560 (30.2)	582/1811 (32.1)	
Revascularization done	154/169 (91.1)	532/582 (91.4)	0.91
3 Vessels	167/560 (29.8)	773/1811 (42.7)	
Revascularization done	149/167 (89.2)	694/773 (89.8)	0.83
Specific native vessels with ≥50% stenosis			
Left main	16/578 (2.8)	79/1895 (4.2)	0.13
LAD	396/568 (69.7)	1463/1862 (78.6)	<0.001
Proximal LAD	168/578 (29.1)	727/1895 (38.4)	<0.001
Left circumflex	294/574 (51.2)	1218/1866 (65.3)	<0.001
Right coronary artery	309/569 (54.3)	1227/1841 (66.6)	<0.001
Any obstructive disease ≥70% stenosis	410/573 (71.6)	1603/1877 (85.4)	<0.001
No. of native vessels with ≥70% stenosis			<0.001
0	158/560 (28.2)	258/1811 (14.2)	
1	199/560 (35.5)	672/1811 (37.1)	
2	143/560 (25.5)	555/1811 (30.6)	
3	60/560 (10.7)	326/1811 (18.0)	
Specific native vessels with ≥70% stenosis			
Left main	7/578 (1.2)	30/1895 (1.6)	0.52
LAD	260/568 (45.8)	1013/1862 (54.4)	<0.001
Proximal LAD	94/578 (16.3)	460/1895 (24.3)	<0.001
Left circumflex	184/574 (32.1)	870/1866 (46.6)	<0.001
Right coronary artery	222/569 (39.0)	911/1841 (49.5)	<0.001
SYNTAX score			<0.001
No.	577	1890	
Median (Q1–Q3)	11 (5–21)	16 (8–25)	
Duke Jeopardy score			<0.001
No.	577	1890	
Median (Q1–Q3)	3 (2–5)	4 (2–5)	

Data are given as number/total (percentage) unless otherwise indicated. CCTA indicates coronary computed tomography angiography; LAD, left anterior descending artery; Q1, quartile 1; and Q3, quartile 3; SYNTAX, Synergy between Percutaneous Coronary Intervention with TAXus and Cardiac Surgery.

severe proximal left anterior descending artery stenosis on CCTA (Duke score 6), there was no difference in the rate of revascularization (percutaneous coronary intervention or coronary artery bypass grafting; 80.5% in women versus 81.9% in men; *P*=0.825). In the same Duke score 6 subgroup, among those who did undergo revascularization, there was no difference in the rate of coronary artery bypass grafting by sex (10 of 33 women [30.3%] versus 103 of 249 men [41.4%]; *P*=0.223; Table S2).

Cardiac Catheterization and Revascularization in the Conservative Strategy Group by Sex

The percentage of women and men randomized to the conservative strategy with at least 1 catheterization during follow-up, whether or not it was in relation to a primary end point event, was similar (26.3% versus 25.6%, respectively; *P*=0.717) (Table 3). There was no difference by sex in the performance of revascularization within the conservative treatment strategy group overall (19.2% versus 21.5%, respectively; *P*=0.242) and excluding revascularization for a suspected primary end point event (Figure 1B). When performed, time to first cardiac catheterization was similar by sex (median [quartile 1–quartile 3] days: 283 [78–653] versus 337 [113–683], respectively; *P*=0.316), and the rate of revascularization was lower among women (72.3% [107/148] versus 82.3% [427/519] of men who underwent cardiac catheterization; *P*=0.007). In both sexes, the reasons for revascularization in the conservative strategy group were mostly either a suspected or a confirmed end point event or refractory angina. Cumulative incidence plots of catheterization and revascularization in the conservative treatment group during follow-up are presented in Figures S1 and S2.

GDMT by Sex

Women were less likely to meet goals for blood pressure, LDL-C, and aspirin use by the end of the study, but were less likely to smoke (Figure 2; Table 4). The SBP goal of <140 mm Hg was met at the end of the study by 73.6% of women and 77.9% of men (*P*=0.003). The LDL-C goal of <70 mg/dL was met at the end of the study by 50.2% of women and 61.3% of men (*P*<0.001). Women were less likely to be on a high-intensity statin (60.7% versus 64.3%; *P*=0.025), and less likely to be on aspirin or an aspirin alternative (other antiplatelet agent) than men (95.6% versus 97.2%; *P*=0.009) but were similarly likely to be taking a β-blocker (88.0% versus 83.5%; *P*=0.124). Women met fewer medical therapy goals at study end. Women

scored lower on the Morisky-Green-Levine scale assessing adherence to medications (79.1% classified as adherent versus 82.2%; *P*=0.018). Hemoglobin A1c was less likely to be <8% at the end of the trial among women than men, although this was not a specified medical therapy goal (79.5% of women versus 85.3% of men; *P*<0.001). Women were similarly likely than men to be taking an antianginal medication (including β-blockers, calcium channel blockers, and other antianginals) at the end of the study (91.1% versus 90.2%; *P*=0.367), but the number of antianginal medications was higher at the end of the study for women compared with men (Table 4). All of these sex differences were also present at the time of randomization, but the trend toward more antianginal medications among women was not statistically significant at randomization. Results were similar in the subset of patients who underwent CCTA (Table S3), except for similar rates of smoking and medication adherence between women and men in this subset. In the subset who underwent cardiac catheterization with the finding of obstructive CAD, women remained less likely to receive a statin than men, but were similarly likely to receive aspirin and high-intensity statin therapy. Still, women were less likely to reach the trial goal of LDL-C <70 mg/dL or to attain a high level of medical therapy optimization,

Table 3. Use of Catheterization and Revascularization in Participants Randomized to the Conservative Strategy Group by Sex

Characteristic	Women (N=562)	Men (N=2029)	*P* value
Participants with at least 1 catheterization during follow-up	148/562 (26.3)	519/2029 (25.6)	0.72
Time from randomization to first catheterization, d	283 (78–653)	337 (113–683)	0.32
Participants with at least 1 revascularization	108/562 (19.2)	436/2029 (21.5)	0.24
Participants with at least 1 revascularization other than for a suspected primary end point event	70/488 (14.3)	269/1751 (15.4)	0.58
Time from randomization to first revascularization, d	282 (72–613)	317 (108–684)	0.23
First revascularization was PCI	78/108 (72.2)	291/436 (66.7)	0.28
Time from randomization to first PCI, d	282 (68–645)	288 (93–656)	0.44
Drug-eluting stent placed	66/78 (84.6)	252/287 (87.8)	0.46
First revascularization was CABG	30/108 (27.8)	145/436 (33.3)	0.28
Time from randomization to first CABG, d	288 (112–596)	347 (137–715)	0.37
IMA graft placed during CABG	0/30 (0.0)	0/145 (0.0)	N/A
Indication for first revascularization			0.46
Suspected event	32/108 (29.6)	119/436 (27.3)	
CEC confirmed event	29/108 (26.9)	133/436 (30.5)	
Failure of GDMT/refractory angina	13/108 (12.0)	34/436 (7.8)	
Nonadherence/other	34/108 (31.5)	150/436 (34.4)	
Participants with at least 1 catheterization or revascularization during follow-up	149/562 (26.5)	528/2029 (26.0)	0.82
Time from randomization to first catheterization or revascularization, d	270 (75–645)	327 (106–670)	0.34
Catheterization or revascularization performed within 90 d of randomization	40/562 (7.1)	119/2029 (5.9)	0.27
Intended management strategy after first diagnostic catheterization in participants with a catheterization, n	41	92	
Medical therapy only	36/41 (87.8)	62/92 (67.4)	0.01
Reason for medical therapy			0.07
No obstructive CAD	29/36 (80.6)	36/62 (58.1)	
Anatomy not suitable for any mode of revascularization	4/36 (11.1)	16/62 (25.8)	
Patient preference	3/36 (8.3)	5/62 (8.1)	
Other	0/36 (0.0)	5/62 (8.1)	
PCI/CABG/hybrid	1/41 (2.4)	21/92 (22.8)	
Undecided	3/41 (7.3)	7/92 (7.6)	
Unknown	1/41 (2.4)	2/92 (2.2)	
Missing	0/41 (0.0)	0/92 (0.0)	

Data are given as number/total (percentage) or median (25th–75th percentile). CABG indicates coronary artery bypass grafting; CAD, coronary artery disease; CEC, clinical events adjudication committee; GDMT, guideline-directed medical therapy; IMA, internal mammary artery; and PCI, percutaneous coronary intervention.

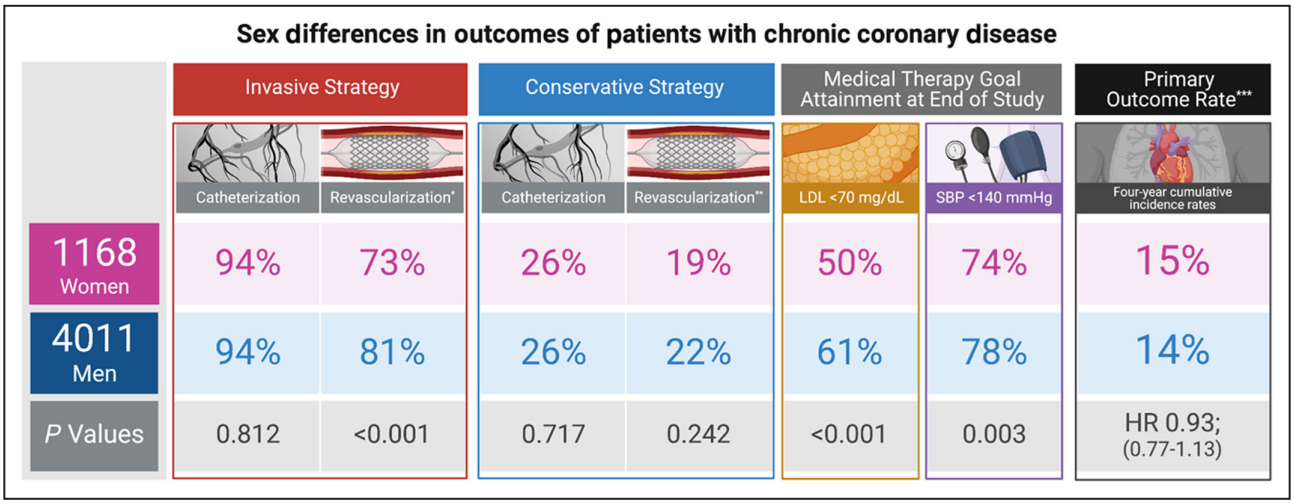

Figure 2. Sex differences in management and outcomes of patients with chronic coronary disease in the ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) trial.
*No sex differences in revascularization rates when stratified by number of vessels diseased on coronary angiography, invasive group. **Revascularization in 72.3% of those undergoing catheterization in conservative group among women, 82.3% among men (*P*=0.007). ***The primary composite outcome included cardiovascular death, myocardial infarction, hospitalization for heart failure, unstable angina, or resuscitated cardiac arrest. The use of invasive procedures, medical therapy goal attainment, and the primary outcome event rate were compared by participant sex in the ISCHEMIA trial. The use of cardiac catheterization was similar for women and men in both the routine invasive strategy group and the conservative strategy group. The rate was far lower in the conservative strategy group in which catheterization was reserved for failure of medical therapy. The rate of revascularization was far lower for women in the invasive group. However, there was no sex difference in revascularization after stratifying for the lower number of vessels diseased on coronary angiography in women (see Table 2 for details). In the conservative strategy group, overall revascularization rates were similar, but among those who had catheterization, revascularization was lower among women (**). Women were less likely to reach the low-density lipoprotein (LDL) and systolic blood pressure (SBP) treatment goals. The primary outcome event rate was similar for women and men. HR indicates hazard ratio. Created with BioRender.com.

and fewer risk factor goals were met among women. However, scores on the Morisky-Green-Levine medication adherence scale indicated similar frequency of adherence for women and men (Table S4).

Trial Primary and Secondary Outcomes by Sex

There were no significant differences in the main treatment effect by sex in the primary composite outcome (adjusted HR for women versus men, 0.93 [95% CI, 0.77–1.13]; *P*=0.465) or the major secondary outcome of cardiovascular death or MI (adjusted HR, 0.93 [95% CI, 0.76–1.14]; *P*=0.494) (Figure 3; Table 5). There was also no difference by sex in MI overall (adjusted HR, 0.82 [95% CI, 0.64–1.04]; *P*=0.101), but the rate of periprocedural MI was lower among women (adjusted HR, 0.40 [95% CI, 0.21–0.76]; *P*=0.005), consistent with lower rates of revascularization among women. When considering only women and men in the invasive strategy group who underwent revascularization, there was no difference in the 4-year rate of procedural MI, 1.8% (95% CI, 0.4%–5.8%) among women versus 2.8% among men (95% CI, 1.6%–4.5%) (*P*=0.514). The effect of CAD severity (≥50%) on MI risk did appear to vary significantly by sex (*P*=0.018; Table S5). There were no significant interactions between participant sex and age, magnitude/extent of ischemia, or diabetes on clinical outcomes. Bleeding rates reported by sites through discharge were not different by sex (3.5% in women and 4.2% in men; *P*=0.317).

There was no significant interaction between sex and treatment strategy for the primary outcome, the major secondary outcome, mortality (both cardiac and all cause), or MI. The *P* value for interaction between sex and treatment on stroke was 0.044, with relatively greater hazard for these outcomes in the invasive group among women than men and lower hazard for women compared with men in the conservative strategy group (Table S6).

Chest Pain Admissions During Follow-Up

Women experienced more emergency department admissions for noncardiac chest pain than men (38/1168 [3.3%] versus 74/4011 [1.8%]; *P*=0.004), but a similar number of hospitalizations for noncardiac chest pain (22/1168 [1.9%] versus 54/4011 [1.3%]; *P*=0.179).

DISCUSSION

In the ISCHEMIA trial, women and men experienced similar rates of the primary and secondary outcomes. Women assigned to the invasive treatment strategy

Table 4. Medical Therapy for Randomized Participants at Baseline and End of Study by Sex

Medical therapy characteristics	Baseline			End of Study*		
	Women (N=1168)	Men (N=4011)	*P* value	Women (N=1168)	Men (N=4011)	*P* value
On guideline-directed medical therapy						
Not smoking	1057/1167 (90.6)	3477/4007 (86.8)	<0.001	1007/1091 (92.3)	3355/3738 (89.8)	0.01
Systolic blood pressure<140 mm Hg	725/1164 (62.3)	2635/3986 (66.1)	0.016	819/1113 (73.6)	2999/3849 (77.9)	0.003
LDL-C<70 mg/dL	287/1116 (25.7)	1334/3824 (34.9)	<0.001	553/1102 (50.2)	2316/3781 (61.3)	<0.001
On aspirin or aspirin alternative	1085/1146 (94.7)	3787/3922 (96.6)	0.004	1033/1080 (95.6)	3630/3734 (97.2)	0.009
On high-intensity statin therapy	377/1106 (34.1)	1534/3834 (40.0)	<0.001	681/1122 (60.7)	2492/3873 (64.3)	0.03
On ACE inhibitor/ARB†	742/1022 (72.6)	2376/3266 (72.7)	0.927	729/981 (74.3)	2351/3152 (74.6)	0.86
On β-blocker†	170/189 (89.9)	738/834 (88.5)	0.567	162/184 (88.0)	677/811 (83.5)	0.12
No. of goals met‡			<0.001			<0.001
0	2/1111 (0.2)	6/3801 (0.2)		1/1072 (0.1)	3/3658 (0.1)	
1	38/1111 (3.4)	157/3801 (4.1)		24/1072 (2.2)	69/3658 (1.9)	
2	376/1111 (33.8)	1091/3801 (28.7)		194/1072 (18.1)	482/3658 (13.2)	
3	536/1111 (48.2)	1738/3801 (45.7)		488/1072 (45.5)	1513/3658 (41.4)	
4	159/1111 (14.3)	809/3801 (21.3)		365/1072 (34.0)	1591/3658 (43.5)	
High level of medical therapy optimization§	159/1111 (14.3)	809/3801 (21.3)	<0.001	365/1072 (34.0)	1591/3658 (43.5)	<0.001
On aspirin or aspirin alternative/other antiplatelet among all participants	1106/1167 (94.8)	3872/4007 (96.6)	0.003	1076/1123 (95.8)	3768/3872 (97.3)	0.010
LDL-C<70 mg/dL and on a statin	281/1116 (25.2)	1318/3822 (34.5)	<0.001	543/1098 (49.5)	2286/3777 (60.5)	<0.001
On ACE inhibitor/ARB among all participants	788/1168 (67.5)	2628/4005 (65.6)	0.241	791/1123 (70.4)	2678/3873 (69.1)	0.41
On statin	1087/1168 (93.1)	3817/4006 (95.3)	0.003	1049/1123 (93.4)	3706/3874 (95.7)	0.002
On antianginal medications‖	1060/1168 (90.8)	3641/4005 (90.9)	0.869	1023/1123 (91.1)	3495/3875 (90.2)	0.37
No. of antianginal medications‖			0.479			0.002
1	454/1060 (42.8)	1674/3641 (46.0)		469/1023 (45.8)	1797/3495 (51.4)	
2	430/1060 (40.6)	1404/3641 (38.6)		397/1023 (38.8)	1243/3495 (35.6)	
3	148/1060 (14.0)	471/3641 (12.9)		128/1023 (12.5)	356/3495 (10.2)	
4	24/1060 (2.3)	76/3641 (2.1)		21/1023 (2.1)	89/3495 (2.5)	
≥5	4/1060 (0.4)	16/3641 (0.4)		8/1023 (0.8)	10/3495 (0.3)	
HbA1c<8%	578/762 (75.9)	2245/2677 (83.9)	<0.001	667/839 (79.5)	2516/2950 (85.3)	<0.001
Adherent to medications based on Morisky-Green-Levine assessment	808/1127 (71.7)	2864/3840 (74.6)	0.052	874/1105 (79.1)	3117/3791 (82.2)	0.02

Data are given as number/total (percentage). ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; HbA1c, hemoglobin A1C; and LDL-C, low-density lipoprotein cholesterol.

*For each individual guideline-directed medical therapy (GDMT) goal, the last visit is defined as the latest visit (at least 12 months after randomization) where the goal is evaluable. If the latest visit where the goal is evaluable is <12 months after randomization, then the individual GDMT goal is missing.

†Participants who are not indicated for ACE inhibitor/ARBs or β-blockers are counted as having missing data for the individual goals.

‡The following GDMT goals contribute to the number of goals met: not smoking, systolic blood pressure<140 mm Hg, LDL-C<70 mg/dL and on any statin, and on aspirin or other antiplatelet or anticoagulant. Number of goals met is missing if any of the individual goals are missing.

§High Level of medical therapy optimization is defined as a participant meeting all of the following goals: not smoking, systolic blood pressure<140 mm Hg, LDL-C<70 mg/dL and on any statin, and on aspirin or other antiplatelet or anticoagulant. High level of medical therapy optimization is missing if any of the individual goals are missing.

‖Includes β blocker, calcium channel blocker, long-acting nitrate, ranolazine, trimetazidine, ivabradine, nicorandil, and other antianginal medications marked as "unknown."

were less likely than men to undergo revascularization because of the lower rate of obstructive CAD at cardiac catheterization and lesser extent of CAD when present. In the conservative treatment strategy group, women and men were equally likely to have cardiac catheterization for a suspected clinical event or failed GDMT, despite higher angina burden and less severe ischemia on stress testing among women at trial entry.[14] Once cardiac catheterization was performed, revascularization was again less likely among women than men. Standardized algorithms were provided to enrolling sites to guide optimization of GDMT and of

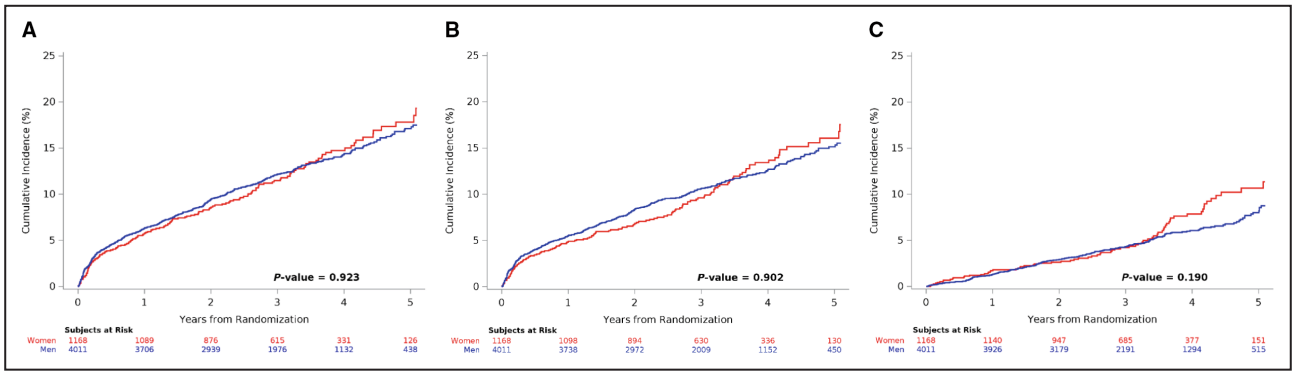

Figure 3. Unadjusted cumulative incidence plot of trial primary and major secondary outcomes and all-cause mortality by sex.

A, Cardiovascular death, myocardial infarction (MI), hospitalization for unstable angina or heart failure, or resuscitated cardiac arrest. **B**, Cardiovascular death or MI. **C**, All-cause death.

complete ischemic revascularization, without regard to sex.[25] Yet, women attained fewer GDMT goals by the end of the study.

The similar clinical outcomes for men and women represent the net effects of sex differences that reflect opposing risks. Women randomized in the ISCHEMIA trial were older than men and had higher rates of hypertension and diabetes with poorer risk factor control throughout follow-up, but had less extensive anatomic CAD and ischemia on imaging. We found the effect of CAD severity of MI varied significantly by sex.

The design of the ISCHEMIA trial is different from the prior clinical outcomes utilizing revascularization and aggressive drug evaluation and the bypass angioplasty revascularization investigation 2 diabetes trials in that randomization of ISCHEMIA trial subjects occurred before diagnostic angiography and there was a higher predefined threshold of ischemia at baseline to qualify for study entry. CCTA was performed before randomization in most patients to confirm the presence of obstructive CAD and to exclude significant left main disease. A similar proportion of women and men had protocol-assigned catheterization in the invasive assigned group. This equal access to cardiac catheterization and revascularization is notable, given that previous studies have demonstrated that women are less likely to undergo further evaluation after a positive functional test result, even within the randomized prospective multicenter imaging study for evaluation of chest pain trial.[33,34] Still, among invasive therapy–assigned patients, fewer women underwent revascularization, largely because of the absence of obstructive CAD at cardiac catheterization. This was the case even though the trial used prerandomization CCTA to confirm obstructive CAD in most participants. This finding is consistent with numerous studies reporting less extensive CAD among women, and with the CCTA findings among randomized participants in this trial, previously reported.[14] When we stratified the invasive group by the number of vessels with at least 50% stenosis, revascularization rates were similar for women and men.

The rates of cardiac catheterization and revascularization by sex within the conservative treatment strategy group were similar, although angina frequency was higher among randomized women compared with randomized men.[14] Whether or not this resulted in worse health status outcomes among women assigned to conservative management will be addressed in ongoing analyses. It is noteworthy, however, that more women experienced chest pain emergency department visits than men, without a difference in adjudicated MI or unstable angina. This pattern is consistent with prior analyses of the relationship between angina severity and the outcomes of cardiovascular hospitalization, MI, and death (namely, more frequent angina in patients with CCD is associated with more angina hospitalizations and heart failure events, but not with increased risk of MI after adjustment for clinical variables).[35,36] Greater angina frequency has also been historically associated with increased rates of revascularization. However, this was not observed in the ISCHEMIA trial, likely because of the study protocol, in which conservative-assigned participants were recommended to undergo revascularization only for symptoms refractory to medical therapy or a suspected end point event. Furthermore, the ISCHEMIA trial excluded patients with an unacceptable level of angina at the time of enrollment.

Despite the rigorous design of the trial and the emphasis on lifestyle intervention and intensive, goal-directed pharmacologic secondary prevention in both arms for all participants, use of GDMT in women was unexpectedly and disappointingly lower than in men throughout study follow-up. Women were less likely to attain blood pressure control, LDL-C targets, and the hemoglobin A1c target. These differences were similar in magnitude when comparing baseline medical

Table 5. Cumulative Incidence Rates and Estimated HRs of Sex for Clinical Outcomes

Event	Women (N=1168)	Men (N=4011)	Unadjusted HR, women vs men (95% CI)	Adjusted* HR, women vs men (95% CI)	*P* value
Cardiovascular death, MI, hospitalization for unstable angina or heart failure, or resuscitated cardiac arrest					
No. of events	151	519	0.99 (0.82–1.18)	0.93 (0.77–1.13)	0.47
Cumulative incidence rate at 4 y (95% CI), %	14.8 (12.4–17.2)	14.3 (13.1–15.6)			
Cardiovascular death or MI					
No. of events	133	457	0.98 (0.81–1.19)	0.93 (0.76–1.14)	0.49
Cumulative incidence rate at 4 y (95% CI), %	13.4 (11.2–15.9)	12.6 (11.5–13.8)			
All-cause death					
No. of events	75	214	1.19 (0.92–1.55)	1.10 (0.84–1.45)	0.48
Cumulative incidence rate at 4 y (95% CI), %	7.9 (6.1–10.1)	6.1 (5.2–7.0)			
Cardiovascular death					
No. of events	59	144	1.40 (1.03–1.89)	1.30 (0.94–1.78)	0.11
Cumulative incidence rate at 4 y (95% CI), %	6.7 (5.0–8.7)	3.9 (3.3–4.7)			
MI					
No. of events	90	353	0.86 (0.68–1.09)	0.82 (0.64–1.04)	0.10
Cumulative incidence rate at 4 y (95% CI), %	8.5 (6.7–10.5)	9.9 (8.8–11.0)			
Nonprocedural MI (type 1, 2, 4b, 4c)					
No. of events	74	252	1.00 (0.77–1.30)	0.95 (0.73–1.24)	0.70
Cumulative incidence rate at 4 y (95% CI), %	7.2 (5.6–9.1)	7.3 (6.4–8.3)			
Procedural MI (type 4a, 5)					
No. of events	11	83	0.45 (0.24–0.85)	0.40 (0.21–0.76)	0.005
Cumulative incidence rate at 4 y (95% CI), %	1.0 (0.5–1.7)	2.2 (1.7–2.7)			
Stroke					
No. of events	22	61	1.23 (0.76–2.01)	1.04 (0.63–1.74)	0.87
Cumulative incidence rate at 4 y (95% CI), %	2.1 (1.3–3.3)	1.7 (1.3–2.2)			
Hospitalization for heart failure					
No. of events	24	52	1.58 (0.97–2.56)	1.54 (0.93–2.58)	0.10
Cumulative incidence rate at 4 y (95% CI), %	1.9 (1.1–2.9)	1.5 (1.1–1.9)			
Cardiovascular death, MI, hospitalization for unstable angina or heart failure, resuscitated cardiac arrest, or stroke					
No. of events	163	559	0.99 (0.83–1.18)	0.93 (0.77–1.11)	0.41
Cumulative incidence rate at 4 y (95% CI), %	16.1 (13.7–18.7)	15.4 (14.1–16.7)			

HR indicates hazard ratio; and MI, myocardial infarction.

*Adjusted for randomized treatment arm, age at randomization, estimated glomerular filtration rate, ejection fraction, and diabetes. Continuous variables are modeled as restricted cubic splines with knots at the 10th, 50th, and 90th percentile of each variable's empirical distribution.

therapy with medical therapy at the end of the study, despite improvement over the course of the study in the cohort in general. For example, the difference in the proportion of patients meeting the LDL-C goal was 9 percentage points lower among women at baseline (25.7% versus 34.9%) and 11 percentage points lower among women at the end of the study (50.2% versus 61.3%). The reasons for this are unclear. Self-reported adherence was modestly lower among women. When we assessed these differences in the subset of patients with obstructive CAD on CCTA, results were largely similar, likely related to the blinded nature of study CCTA in this trial. Interestingly, analysis of the subset of patients within the invasive strategy group who had at least single-vessel CAD, and in the subset with CCTA performed, showed that self-reported adherence to medications was similar between women and men. It has previously been reported that awareness by patients of coronary computed tomography results has the potential to increase adherence.[37] Within the subset of patients in the invasive strategy group with obstructive CAD, high-intensity statin therapy and blood pressure goal attainment were similar by sex. Still, even with the knowledge by both patients and physicians of anatomic details of significant CAD, the LDL-C treatment goal was less likely to be met among women, and women attained fewer medical therapy goals. Although we do not have access to detailed information about dose titration in response to blood pressure and laboratory values in the ISCHEMIA trial, analysis

of the relationship between risk factor goal attainment and outcomes in the trial is ongoing. Nevertheless, the imperative to achieve equitable use of GDMT implementation among women with CCD is both an important challenge and an opportunity for improved clinical outcomes.

We have previously reported that ISCHEMIA trial participants with 3-vessel CAD were at particularly high risk of cardiovascular events, and that the rate of cardiovascular death or MI tended to be lower among invasive strategy–assigned patients than conservative strategy–assigned patients in the most severe CAD subgroup.[38] Interestingly, there was evidence of interaction between sex and CAD severity on the end point of MI, such that women with 3-vessel CAD had higher risk of MI than men, and at lesser extent of CAD, women were at lower risk of MI than men. This raises a question of whether undertreatment of women could have been particularly impactful in those with more extensive CAD. There was also interaction between sex and treatment on stroke, with women at higher risk of stroke in the invasive strategy group, and no difference by treatment group in stroke among men. The interaction test results should be interpreted with caution, especially as adjustment for multiple testing was not performed.

This analysis has several limitations. The ISCHEMIA trial cohort was only 23% female, because of obstructive CAD and moderate or severe ischemia eligibility criteria, which women more often failed to meet.[14] Specific drugs and doses of GDMT were not available. As a randomized trial, we are able to address the effectiveness of alternative management strategies, but the real-world effectiveness will require different types of studies. Heath status outcomes will be reported separately.

CONCLUSIONS

Despite a higher angina burden and less obstructive CAD, women and men with CCD and site-assessed moderate or severe ischemia in the ISCHEMIA trial experienced similar adjusted rates of the primary and secondary outcomes during 3.2-year median follow-up. Cardiac catheterization was used at similar rates by sex, but revascularization was less frequent among women, because of the higher prevalence of ischemia with no obstructive coronary arteries and lesser extent of CAD at angiography. Disappointingly, medical therapy goal attainment was lower among women than men, which represents an important challenge and opportunity for improvement.

APPENDIX A

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
			(If Applicable)	
United States (853)*				
Country Leader				
David J. Maron, MD				
Regional Leader for VA Sites				
William E. Boden, MD				
	Kreton Mavromatis, MD	John Doan, MD	Decatur, GA	Atlanta VA Medical Center (139)
	Jason Linefsky, MD	Raven Lee, CCRP		
		Risha Patel		
	Todd Miller, MD	So Yang Cho	Rochester, MN	Mayo Clinic (50)
		Susan Milbrandt		
		Dawn Shelstad		
	Subhash Banerjee, MD	Preeti Kamath, BDS, MHA, CCRP	Dallas, TX	V.A. North Texas Health Care System (35)
		Ishita Tejani, BDS, MS, MSPH		
	Harmony R. Reynolds, MD	Stanley E. Cobos, BA	New York, NY	NYU Langone Medical Center-Bellevue Hospital (26)
	Jonathan D. Newman, MD, MPH	Kirsten J. Quiles, MS		
	Sripal Bangalore, MD	Raven R. Dwyer, MPH		
	Robert M. Donnino, MD	Dalisa Espinosa, MBS		
	Lawrence M. Phillips, MD			

APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Muhamed Saric, MD, PhD			
	Khaled Abdul-Nour, MD	Allison Schley, BS	Detroit, MI	Henry Ford Health System (21)
		Heather Golden		
	Peter H. Stone, MD	Hermine Osseni, MS	Boston, MA	Brigham and Women's Hospital, Harvard Medical School (21)
		Charlene Wiyarand		
		Peter Douglass, BA		
		Hayley Pomeroy, BA		
		Alexandra Craft, BA		
		Bethany Harvey, BA		
	James J. Jang, MD	Olivia Anaya	San Jose, CA	Kaiser Permanente San Jose (18)
	Gennie Yee, MD	Phoebe Goold, RN		
	Steven Weitz, MD	Steven Giovannone	Schenectady, NY	Cardiology Associates of Schenectady P.C. (17)
		Lori Pritchard, RN		
	Suzanne Arnold, MD	Rosann Gans, RN	Kansas City, MO	Saint Luke's Hospital (17)
	James Henry O'Keefe, Jr, MD (PI from 2012 to 2016)	Paul Kennedy, RN		
	Michael D. Shapiro, DO	Shobana Ganesan, PhD	Portland, OR	Oregon Health and Science University (17)
		David Schlichting, LPN		
		Aynun Naher		
	Mohammad El-Hajjar, MD		Albany, NY	Albany Medical Center Hospital (16)
	Mandeep S. Sidhu, MD, MBA			
	Steven A. Fein, MD	Wendy L. Stewart, MS		
	Mikhail T. Torosoff, MD, PhD	Kristin M. Salmi, BS		
	Radmila Lyubarova, MD			
	Sulagna Mookherjee, MD			
	Krzysztof Drzymalski, MD			
	Edward O. McFalls, MD, PhD		Minneapolis, MN	Minneapolis VAMC (15)
	Santiago A. Garcia, MD			
	Stefan C. Bertog, MD	Debra K. Johnson, RN		
	Rizwan A. Siddiqui, MD	Rebekah R. Herrmann, RN		
	Areef Ishani, MD			
	Ronnell A. Hansen, MD			
	Michel Georges Khouri, MD	Kristine Arges	Durham, NC	Duke University Medical Center (15)
		Melissa LeFevre		
		Jennifer Tomfohr		
	Jonathan L. Goldberg, MS, MD	Kimberly Ann Byrne	Cleveland, OH	Louis Stokes Cleveland Veterans Affairs Medical Center (14)
		Taissa Zappernick		
	Richard Goldweit, MD	Sallie Canada	Englewood, NJ	Englewood Hospital and Medical Center (13)

(*Continued*)

APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
		Meghana Kakade		
		Patricia Mieses		
		Stanley E. Cobos, BA	Brooklyn, NY	NYU-HHC Woodhull Hospital (12)
		Raven R. Dwyer, MPH		
	Ronny A. Cohen, MD	Dalisa Espinosa, MBS		
	Brooks Mirrer, MD	Kirsten J. Quiles, MS		
	Victor Navarro, MD	Magdalena Rantinella, BS		
		Jessica Rodriguez, BS		
		Olivia Mancilla, BS		
	David E. Winchester, MD, MS	Susan Stinson, RN	Gainesville, FL	Malcom Randall VAMC (11)
	Marvin Kronenberg, MD	Terry Weyand	Nashville, TN	Vanderbilt University Medical Center (11)
	Philip Rogal, MD	Sherron C. Crook		
	Christopher McFarren, MD			
	John F. Heitner, MD	Jean Ho	Brooklyn, NY	New York-Presbyterian/ Brooklyn Methodist Hospital (10)
		Saadat Khan		
		Mahmoud Mohamed		
	Ira M. Dauber, MD	Mary R. Soltau, RN	Littleton, CO	South Denver Cardiology Associates, P.C. (10)
		Delsa K. Rose, RN		
		Rebecca J. Wimmer, RN		
		Kathy E. Siegel, RN		
		Susan Derbyshire		
	Charles Cannan, MD	Michelle Dixon	Portland, OR	Providence Heart and Vascular Institute (10)
		Gerald Leonard		
	Sriram Sudarshan, MD	Ciarra Heard, LVN	Wichita Falls, TX	Wichita Falls Heart Clinic (9)
		Viviana Gabriel, LVN		
		Sukie Desire		
	Puja K. Mehta, MD		Atlanta, GA	Emory University (9)
	Michael McDaniel, MD	Fauzia Rashid, PhD		
	Stamatios Lerakis, MD	Senait Asier		
	Arshed Quyyumi, MD	Keyur Patel		
	Nanette K. Wenger, MD			
	Chester M. Hedgepeth, MD, PhD	Jennifer Gillis, APRN	Warwick, RI	Kent Hospital (9)
	Heather Hurlburt, MD	Megan Manocchia, RN		
	Alan Rosen, MD	Susan Moore, RN		
		Elizabeth Congdon		
	Zakir Sahul, MD	Gail Brandt	Ypsilanti, MI	Michigan Heart, PC (9)
		Nora Marchelletta		
		Kristina Wippler		
	David Booth, MD	Yvonne Taul, RN	Lexington, KY	University of Kentucky (8)
	Steve Leung, MD	Jennifer Isaacs, MS		
	Ahmed Abdel-Latif, MD, PhD	Viktoria Bulkley, RN		
	Hassan Reda, MD	Caroline Rodgers		

(*Continued*)

APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Khaled Ziada, MD			
	Sampoornima Setty, MD	Kimberly E. Halverson, RHIT	La Crosse, WI	Gundersen Lutheran Medical Center (8)
		Christine Roraff, RN		
		Jonean Thorsen, RN		
	Rajat S. Barua, MD, PhD	Amarachi Ojajuni	Kansas City, MO	Kansas City VA Medical Center (8)
		Oni Olurinde		
		Kamalakar Surineni		
	Fadi Hage, MD	Badhma Valaiyapathi, MD	Birmingham, AL	UAB Vascular Biology and Hypertension Program (8)
	Christiano Caldeira, MD			
	James E. Davies, MD			
	Massoud Leesar, MD			
	Jaekyeong Heo, MD			
	Amy Iskandrian, MD			
	Firas Al Solaiman, MD			
	Satinder Singh, MD			
	Khaled Dajani, MD	Carol M. Kartje, BSN	Maywood, IL	Loyola University Medical Center (8)
	Mohammad El-Hajjar, MD		Albany, NY	Samuel Stratton VA Medical Center of Albany NY (7)
	Paul Der Mesropian, MD			
	Joseph Sacco, MD	Michele Rawlins, NP		
	Brian McCandless, MD	Jennifer Thomson, MA		
	Marisa Orgera, MD			
	Mandeep S. Sidhu, MD, MBA (2012–2016)			
		Mary Colleen Rogge, RN	Cincinnati, OH	Cincinnati VA Medical Center (7)
	Imran Arif, MD	Julie Bunke, BA		
	Hanan Kerr, MD	Kendra Unterbrink, PA		
		Jacqueline Fannon, RN		
		Cynthia Burman, NP		
	Jorge F. Trejo (Gutierrez), MD	Marcia F. Dubin, CCRP	Jacksonville, FL	Mayo Clinic Florida (7)
	Gerald Fletcher, MD			
	Gary E. Lane, MD			
	Lynn M. Neeson, DNP			
	Pragnesh P. Parikh, MD			
	Peter M. Pollak, MD			
	Brian P. Shapiro, MD			
	Kevin Landolfo, MD			
	Anthony Gemignani, MD	Sarah Beaudry, RN	White River Junction, VT	VAMC-White River Junction (7)
	Daniel O'Rourke, MD			
	Judith L. Meadows, MD	Stephanie A. Tirado, RN	West Haven, CT	VA Connecticut Healthcare System (7)
		Janet Halliday		
		Pamela Julian		

(*Continued*)

APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Jason T. Call, MD	Stephanie, M. Lane, RN, BSN, CCRN	Winchester, VA	Winchester Cardiology and Vascular Medicine, PC (7)
		Jennifer L. Stanford, RN, MSN		
	Joseph Hannan, MD		Worcester, MA	Saint Vincent Hospital at Worcester Medical Center (7)
	Robert Bojar, MD	Patricia Arsenault, RN		
	Deepti Kumar, MD	Pamela Sigel, RN		
	John Mukai, MD			
	Edward T. Martin, MS, MD	Miriam Brooks	Tulsa, OK	Oklahoma Heart Institute (7)
	Gabriel Vorobiof, MD	Ladda Douangvila	Los Angeles, CA	Ronald Reagan UCLA Medical Center (7)
		Rubine Gevorgyan		
	Alec Moorman, MD	Fatima Ranjbaran, RN	Seattle, WA	University of Washington Medical Center (7)
		Bryn Smith, BS		
		Carly Ohmart		
	Scott Kinlay, MBBS, PhD		West Roxbury, MA	VA Boston Healthcare System (6)
	Robert J. Hamburger, MD			
	Thomas P. Rocco, MD	Samantha Ly, MA		
	Deepak L. Bhatt, MD, MPH	Margot C. Quinn, BA		
	Kevin Croce, MD, PhD	Sara Temiyasathit, PhD		
	Jacquelyn A Quin, MD	Jacquelyn Do, MPH		
	Jati Anumpa, MD	Desiree Tobin, MPH		
	Marco Zenati, MD, MSc			
	David P Faxon, MD			
	Glenn Rayos, MD	Jennifer Langdon	Daytona Beach, FL	Daytona Heart Group (6)
		Marcia Werner Bayer		
	Ashraf Seedhom, MD	Amanda O'Malley	Albany, NY	Capital Cardiology Associates (6)
	Lance Sullenberger, MD	Erin Orvis		
	Gregory Kumkumian, MD	Mandy Murphy, RN	Bethesda, MD	NIH Heart Center at Suburban Hospital (6)
		Ann Greenberg, RN		
		Margaret Iraola, RN		
	Steven P. Sedlis, MD	Leandro C.Maranan, CCRC	New York, NY	VA New York Harbor Health Care System (6)
	Robert M. Donnino, MD			
	Jeffrey Lorin, MD			
	Jacqueline E. Tamis-Holland, MD	Ammy Malinay, RN	Ridgewood, NJ	Mount Sinai Saint Luke's Hospital (6)
	Robert Kornberg, MD			
	Robert Leber, MD			
	Souheil Saba, MD	Candice P. Edillo, RN	Southfield, MI	Providence-Providence Park Hospital (6)
	Michael W. Lee, MD			
	Delano R. Small, MD			
	Wassim Nona, MD			

(*Continued*)

APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Patrick B. Alexander, MD			
	Iram Rehman, MD			
	Umesh Badami, MD	Ann Ostrander, RN	Saginaw, MI	Covenant Medical Center, Inc (5)
		Stephanie Wasmiller, RN		
	Kevin Marzo, MD	Wendy Drewes, RN	Mineola, NY	NYU Winthrop (5)
		Dipti Patel, RN		
	Inga H. Robbins, MD		Pomona, NJ	AtlantiCare Regional Medical Center (5)
	Howard A. Levite, MD	Jackie M White, RN, BSN CCRC		
	Sanjay Shetty, MD	Alison Hallam		
	Mayuri Patel, MD			
	Glenn S. Hamroff, MD	Benjamin J Spooner, RPA-C	Cortlandt Manor, NY	NYP Medical Medical Group Hudson Valley Cardiology (5)
		Linda M Hollenweger, LPN,CCRC		
	Raymond W. Little, MD	Holly Little	Houston, TX	Houston Heart and Vascular Associates (5)
	Brandi D. Zimbelman, FNP-C	Tiffany Little		
	Charles Y. Lui, MD	Nona A Eskelson, RN	Salt Lake City, UT	Salt Lake City VA Medical Center (4)
	Brigham R. Smith, MD			
	Daniel P. Vezina, MD, MSC			
	Lillian L. Khor, MBBCh, MSc			
	Josephine D. Abraham, MD, MPH			
	David A. Bull, MD			
	Stephen H. McKellar, MD, MSc			
	David Booth, MD	Yvonne Taul, RN	Lexington, KY	Lexington VA Medical Center (4)
	John Kotter, MD	Caroline Rodgers, RN		
	Ahmed Abdel-Latif, MD, PhD	Jennifer Isaacs, MS		
		Viktoria Bulkley		
	Bob Hu, MD	Renee Kaneshiro	Palo Alto, CA	Palo Alto Medical Foundation Research Institute (4)
	Arthur J. Labovitz, MD		Tampa, FL	University of South Florida (4)
	Michael Berlowitz, MD	Bonnie J. Kirby, RN, MSN		
	Philip Rogal, MD	Nhi N. Tran, MS		
	Christopher McFarren, MD	Catherine Jahrsdorfer, RN, BSN		
	Fadi Matar, MD			
	Christiano Caldeira, MD			
	David J. Maron, MD		Stanford, CA	Stanford University School of Medicine (4)
	Fatima Rodriguez, MD, MPH	Reem Yunis, PhD		
	Ingela Schnittger, MD	Jhina Patro		
	William F. Fearon, MD			

(*Continued*)

APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Prakash Deedwania, MD	Antonia Vega	Fresno, CA	UCSF-Fresno Community Regional Medical Center (4)
	Kiran Reddy, MD			
	Joseph Sweeny, MD	Hugo Bloise-Adames	New York, NY	Icahn School of Medicine at Mount Sinai (4)
		Santa Jimenez		
		Nicole Saint Vrestil		
		Reyna Bhandari		
	Christopher Spizzieri, MD	Danielle Schade	Camp Hill, PA	Holy Spirit Hospital Cardiovascular Institute (4)
		Roxanne Yost		
	Claudia P Hochberg, MD	Paula Beardsley	Boston, MA	Boston Medical Center (4)
		Denise Fine		
	William D. Salerno, MD	Jana Tancredi, RN, MA/MSN, CCRN	Saddle Brook, NJ	Hackensack University Medical Center (4)
		Patricia Arakelian		
		Susan Mathus		
		Deborah O'Neill		
	Ray Wyman, MD	Joy Burkhardt, CCRP	Torrance, CA	Torrance Memorial Medical Center (4)
		Suellen Hosino, RN, BSN, CCRP		
		Oksana A. Lubyanaya, BA	Santa Ana, CA	Coastal Heart Medical Group (4)
		Jose D. Salas, BS		
	Amer Zarka, MD	Maria Aguirre		
	Anil V. Shah, MD	Manu Dhawan		
		Diana Parra		
		Tri Tran		
	Thomas Haldis, DO	Catherine Weick, BSRT(R)(VI)	Fargo, ND	Sanford Health (4)
		Katie Fowler-Lehman, BSN		
		Natalie Spitzer, BSN		
		Casey Riedberger		
		Catherine Weick		
	Jeffrey A. Kohn, MD	Stanley E. Cobos, BA	New York, NY	NYU New York Medical Associates (4)
		Raven R. Dwyer, MPH		
		Dalisa Espinosa, MBS		
		Kirsten J. Quiles, MS		
	Saket Girotra, MD	Carrie Drum, RN	Iowa City, IA	University of Iowa Hospitals and Clinics (4)
		Kimberly Miller-Cox, RN		
		Amy Ollinger, RN		
	Omar Almousalli, MD	Elizabeth Capasso-Gulve	Fairview Heights, IL	Advanced Heart Care Group (4)
		Alaine Melanie Loehr		
		Marlowe Mosley		

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APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Mayil S. Krishnam, MD	Shirin Heydari, MS	Orange, CA	University of California Irvine Medical Center (3)
	Jeffrey C. Milliken, MD	Andrea M. Lundeen, MA		
	Pranav M. Patel, MD	Edgar Karanjah, MD		
	Arnold H. Seto, MD	Wanda C. Marfori, MD		
	Kevin T. Harley, MD	Eduardo Hernandez-Rangel, MD		
	Michael A. Gibson, MD	Pam Singh		
	Byron J. Allen, MD			
	Rita Coram, MD	Anne Marie Webb, BSN	Louisville, KY	University of Louisville (3)
		Ellie Fridell, BS		
		Heidi Wilson, BS		
	Sabu Thomas, MD, MSc	Angela Kim, BS	Rochester, NY	University of Rochester (3)
	Ronald G Schwartz, MD, MS	Patrick Wilmot, BS		
	Wei Chen, MD, MS			
	Mahfouz El Shahawy, MD	Ramona Stevens	Sarasota, FL	Cardiovascular Center of Sarasota (3)
	James Stafford, MD	Loriane Black	Baltimore, MD	University of Maryland Medical Center (3)
	William B. Abernethy, MD	Amber B. Hull, RN	Asheville, NC	Asheville Cardiology Associates (3)
		Olivia J. Lim, RN		
		Helen C. Tucker		
		Natasha C. Putnam, RN		
		Linda L. Hall		
		Tia Cauthren		
		Trish Tucker		
	Andrew Zurick, MD	Hollie Horton	Nashville, TN	Saint Thomas Hospital (3)
		Jan Orga		
	Thomas M. Meyer, MD	Joyce R. White, MSN NP-C	Lynchburg, VA	Stroobants Cardiovascular Center (3)
	Ronald G. Morford, MD	Cynthia Baumann, RN		
	Bruce Rutkin, MD	Vidya Seeratan	Manhasset, NY	Northwell Health-Manhasset (3)
	Sabahat Bokhari, MD	Magnolia Jimenez	New York, NY	Columbia University Medical Center (3)
	Seth I. Sokol, MD	Cidney Schultz, RN	Bronx, NY	Jacobi Medical Center (3)
	Jay Meisner, MD	Jeanne Russo, RN		
	Ihab Hamzeh, MD		Houston, TX	Baylor College of Medicine (3)
	Arunima Misra, MD	Zohra Huda, RN, BSN, CCRP		
	Matthew Wall Jr., MD	Araceli Boan		
	Veronica Lenges De Rosen, MD			
	Mahboob Alam, MD			
	Michael C. Turner, MD	Christine R Hinton	Lake Charles, LA	Cardiovascular Specialists of Southwest Louisiana (3)
	Thomas J. Mulhearn, MD			
	Arnold P. Good, MD	Beth A. Archer, BSN, RN	Columbus, OH	Ohio Health Grant Medical Center (3)

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APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
		Julia S. Dionne, BA		
		Cheryl A. Allardyce, BSN, RN		
		Lindsey N. Sikora, BSN, RN		
		Jennifer H. Czerniak, RN		
		Jennifer A. Mull, MSN, RN		
		Elizabeth Ferguson		
		Frances Laube		
	Nicolas W. Shammas, MD, MS	Gail A Shammas, BSN, RN	Davenport, IA	Midwest Cardiovascular Research Foundation (3)
		Lori Christensen		
		Holly Park		
	Robert Chilton, MD	Joan Hecht	San Antonio, TX	Audie Murphy V.A. (2)
	Patricia K. Nguyen, MD	Davis Vo, BS	Palo Alto, CA	VA Palo Alto Healthcare System (2)
		James Hirsch		
	Matthew Jezior, MD	Jody Bindeman	Bethesda, MD	Walter Reed National Military Medical Center (2)
		Sara Salkind		
		Dalisa Espinosa, MBS	Providence, RI	Miriam Hospital (2)
		Lori-Ann Desimone, BSN		
	Paul C. Gordon, MD	Lina Felix-Stern		
	Thomas Crain, MD	Jassira Gomes		
		Catherine Gordon, BSN		
	Robert Stenberg, MD	Aimee Mann	Johnstown, PA	Conemaugh Valley Memorial Hospital (2)
		Theresa McCreary		
	Ronald P. Pedalino, MD	Stanley E. Cobos, BA	Brooklyn, NY	NYU-HHC Kings County Hospital Center (2)
		Raven R. Dwyer, MPH		
		Dalisa Espinosa, MBS		
		Kirsten J. Quiles, MS		
	Joseph Wiesel, MD	Stanley E. Cobos, BA	Flushing, NY	New York University - Langone Cardiovascular Associates (2)
		Raven R. Dwyer, MPH		
		Dalisa Espinosa, MBS		
		Kirsten J. Quiles, MS		
	George J. Juang, MD	Candace Gopaul, BS	Brooklyn, NY	Coney Island Hospital (2)
		Karen Hultberg		
		Tauqir Huk		
		Afshan Hussain		
	Mohammed Al-Amoodi, MD	Yesenia Zambrano, BS	Yuma, AZ	Yuma Regional Medical Center (2)
		Sarah Medina Rodriguez		
		Trudie Milner		
	David Wohns, MD	Abbey Mulder, RN	Grand Rapids, MI	Spectrum Health (2)
		Stacie Van Oosterhout, MEd		
	Ellis W. Lader, MD	Martha Meyer, RN, MSN	Kingston, NY	Mid Valley Cardiology (1)

(*Continued*)

APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Michael Mumma, MD	Nancy L. Clapp, RN, BA, CCRC	Sarasota, FL	Sarasota Memorial Hospital (1)
		Heather Barrentine		
	Lekshmi Dharmarajan, MD	Jenne M. Jose, PA	Bronx, NY	NYU-HHC Lincoln Medical and Mental Health Center (1)
		Stanley E. Cobos, BA		
		Raven R. Dwyer, MPH		
		Dalisa Espinosa, MBS		
		Kirsten J. Quiles, MS		
		Jenne Manchery		
	Joseph F.X. McGarvey Jr, MD	Vera McKinney, RN	Doylestown, PA	Doylestown Health Cardiology (1)
		Linda Schwarz, RN		
	Thomas R. Downes, MD (till Dec. 2016)	Scott M. Kaczkowski	Loveland, CO	Medical Center of the Rockies (1)
	Gary J. Luckasen, MD (from Dec. 2016)	Adam J. Jaskowiak		
		Joel Klitch		
	Benjamin Cheong, MD	Debra Dees	Houston, TX	Baylor St. Luke's Medical Center (1)
	Srinivasa Potluri, MD	Precilia Vasquez	Plano, TX	Baylor Research Institute at Legacy Heart Center (1)[†]
	Ronald A. Mastouri, MD		Indianapolis, IN	Indiana University/ Krannert Institute of Cardiology (1)
	Jeffery A. Breall, MD, PhD	Elise L. Hannemann, RN,CCRC		
	George E. Revtyak, MD	Judy Mae Foltz, RN,CCRC		
	Jonathan W. Bazeley, MD			
	Dayuan Li, MD	Emily DeRosa	St. Paul, MN	HealthEast Saint Joseph's Hospital (1)
		Beth Jorgenson		
		Joyce Riestenberg-Smith		
	Kenneth Giedd, MD		New York, NY	Beth Israel Medical Center (1)
	Wayne Old, MD	Rebecca Bariciano	Chesapeake, VA	Cardiovascular Associates, Ltd (1)
	Francis Burt, MD		Bethlehem, PA	Saint Luke's Hospital and Health Network (1)
	Kozhaya Sokhon, MD	Jessica Waldron	Sugar land, TX	Medicus Alliance Clinical Research Org, Inc (1)
		Michelle Mayon		
	Deepika Gopal, MD		Plano, TX	The Heart Hospital Baylor (1)
	Uma S. Valeti, MD	Gretchen Ann Peichel, RN	Minneapolis, MN	University of Minnesota (1)
	Jon Kobashigawa, MD	Brandy Starks	Beverly Hills, CA	Cedars Sinai Medical Center (1)
		Lucilla Garcia		
		Maria Thottam		
India (941)				
Country Leader				

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
Balram Bhargava, DM				
		Anjali Anand, MSc	Calicut	Government Medical College (208)
	Sajeev Chakanalil Govindan, MD, DNB, DM, PhD	Janitha Raj, B.Tech		
	Rajesh Gopalan Nair, MD, DNB, DM	Reshma Ravindran, MSc		
		Rajalekshmi VS, MSc, MScCRRA		
	Cholenahally Nanjappa Manjunath, MD, DM	Nandita Nataraj, BE(Biotech) PGDICRCDM	Bengaluru	Sri Jayadeva Institute of Cardiovascular Sciences and Research (149)
	Nagaraja Moorthy, MD, DM	Soundarya Nayak, BE(Biotech) PGDICRCDM		
	Satvic Cholenahally Manjunath, MD,DM	Mahevamma Mylarappa, GNM (General Nursing)		
	Suryaprakash Narayanappa, MBBS			
	Neeraj Pandit, MD, DM	Sheromani Bajaj	New Delhi	Dr Ram Manohar Lohia Hospital (101)
	Ranjit Kumar Nath, MD, DM	Vandana Yadav, Msc,PGDACR		
		Girish Mishra, Msc, PGDACR		
	S.K. Dwivedi, DM	Roma Tewari, PG	Lucknow	King George's Medical University, Department of Cardiology (100)
	V.S. Narain, DM	Meenakshi Mishra, PG		
	Sharad Chandra, DM	Shivali Patel		
		Suman Singh, PG		
	Gurpreet S. Wander, DM		Ludhiana	Hero DMC Heart Institute, Dayanand Medical College and Hospital (83)
	Rohit Tandon, MD			
	Sarju Ralhan, M.Ch (CTVS)	Baljeet Kaur, MSc (Biotechnology)		
	Naved Aslam, DM	Sonika Gupta, MBA, B. Pharmacy		
	Abhishek Goyal, DM			
	Balram Bhargava, DM	Chandini Suvarna, BDS	New Delhi	All India Institute of Medical Sciences (67)
	G.Karthikeyan, DM			
	S.Ramakrishnan, DM			
	Sandeep Seth, DM			
	Rakesh Yadav, DM			
	Sandeep Singh, DM			
	Ambuj Roy, DM			
	Neeraj Parakh, DM			
	Sunil Kumar Verma, DM			
	Rajiv Narang, DM			
	Sundeep Mishra, DM			
	Nitish Naik, DM			
	Gautam Sharma, DM			
	Shiv Kumar Choudhary, M.Ch			
	Chetan Patel, DNB			
	Gurpreet Gulati, MD			

(*Continued*)

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Sanjeev Sharma, MD			
	V. K. Bahl, DM			
	Anoop Mathew, MD	Binoy Mannekkattukudy Kurian	Kolenchery	MOSC Medical College Hospital (39)
	Eapen Punnoose, MD			
	Milind Avdhoot Gadkari, MD	Sheetal Rupesh Karwa, BHMS	Pune	KEM Hospital Pune (35)
	Siddharth Gadage, MD DNB	Suvarna Kolhe, MSc		
	Tapan Umesh Pillay, BHMS MSc			
	Santhosh Satheesh, MBBS, MD, DM	R. J. Vindhya, B.Sc. (Bio-Technology), MSc(Bio-Informatics)	Pondicherry	Jawaharlal Institute of Postgraduate Medical Education and Research (31)
		Peeyush Jain, MD	New Delhi	Fortis Escort Heart Institute
		Ashok Seth, MD		–31
		Zile Singh Meharwal, MD		
	Atul Mathur, MD	Atul Verma, MD		
	Upendra Kaul, MD	Mona Bhatia, MD		
		Ankush Sachdeva, MD		
		Thounaojam Indira Devi, RN		
		Nungshi Jungla, RN		
	Johann Christopher, MD, DNB	K. Manjula Rani, MSc.	Hyderabad	Gurunanak CARE Hospital (27)
	Rajeev Menon, MD, DNB	M. Sowjanya Reddy, BSc		
	Nirmal Kumar, MD, DNB	K. Preethi, BSc		
	Abraham Oomman, MD, DM, DNB	Rinu R sidh, MSc(Clinical Research)	Chennai	Apollo Research and Innovation (23)
	Robert Mao, MD, DM	T. Ramakrishnan, B.Tech(Biotechnology)		
	Hilda Solomon, PhD	Rajesh Francis, MSc(Clinical Research)		
	Sudhir Naik, MD, DM	Vamshi Priya P., MSc	Hyderabad	Apollo Research and Innovations (13)
	Sajeeda Parveen Khan, MBBS, (Dip. Card)			
	Johann Christopher, MD	Kotiboinna Preethi	Hyderabad	CARE Nampally (11)
	Nirmal Kumar, MD			
	Purvez Grant, MD	Shweta Hande, BHMS, PGDCR	Pune	Ruby Hall Clinic, Grant Medical Foundation (10)
		Poonam Sonawane, B.ScMicrobiology, ACCR		
	Ranjan Kachru, MD	Abhishek Dubey	New Delhi	Fortis Healthcare Fl.t Lt. Rajan Dhall Hospital (4)
		Kavita Rawat		
	Ajit Kumar VK, MD, DM		Trivandrum	Sree Chitra Tirunal Institute for Medical Sciences and Technology (3)
	Sanjay Ganapathi, MD, DM			
	Jayakumar K, MS, M.Ch	Vineeth CP		
	Harikrishnan Sivadasanpillai, MD, DM	Manas Chacko, RN		
	Bijulal Sasidharan, MD, DM	Suresh Babu		
	Kapilamoorthy TR, MD			
	Johann Christopher, MD	Sowjanya Reddy	Hyderabad	CARE Hospital (3)

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Praneeth Polamuri, MD	Manjula Rani		
	Upendra Kaul, MD	Priyadarshani Arambam	New Delhi	Batra Hospital and Medical Research Centre (3)
		Bebek Singh		
United Kingdom (539)				
Country Leaders				
Roxy Senior, MBBS, MD, DM				
Keith AA Fox, MBChB *(past)*				
Country Coordinators				
Grace M. Young, MSc, BSc (Hons)				
Kathryn Carruthers *(past)*				
	Roxy Senior, MBBS, MD, DM		Harrow	Northwick Park Hospital Harrow/Royal Brompton Hospital London (202)
	Ahmed Elghamaz, MB BCh			
	Sothinathan Gurunathan, MBChB			
	Nikolaos Karogiannis, MBBS	Grace M. Young, MSc, BSc (Hons)		
	Benoy N Shah, MD, MBBS, BSc (Hons)	Christopher Kinsey		
	Richard HJ Trimlett, MBBS, CCST	Raisa Kavalakkat, MSc, BSc, RN		
	Michael B Rubens, LRCP, MRCS, MBBS, DMRD	Jo Evans, RN		
	Edward D Nicol, MD, BMedSci, MBBS, DTM&H	Ikraam Hassan, RN		
	Tarun K Mittal, MD			
	Reinette Hampson, BSc (Hons), BA (Hons)			
	Reto Andreas Gamma, MBBS	Sarah Williams, RN	Chelmsford	Broomfield Hospital (39)
		Kim Holland, RN		
		Karen Swan, RN		
	Mark A de Belder, MD	Bev Atkinson, RN	Middlesbrough	The James Cook University Hospital, Middlesbrough (37)
	Jeet Thambyrajah, MD			
	Thuraia Nageh, BSc(Hons) MBBS MD MRCP	Swapna Kunhunny, MRes Clin Res, BSc (N), RN	Westcliffe on Sea	Southend University Hospital (34)
	John R Davies, MBBS, PhD			
	Steven J. Lindsay, MD	Craig Atkinson, RN	Bradford	Bradford Royal Infirmary (20)
	John Kurian, MD	Carita Krannila, RN		
	Haqeel Jamil, MD	Manitha Vinod, RN		
	Osama Raheem, MD			
	Angela Hoye, MD	Lisa Chaytor	Cottingham	The University of Hull/ Castle Hill Hospital (19)
		Leanne Cox		
		Julie Morrow		
		Kay Rowe		

(*Continued*)

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Patrick Donnelly, MD	Stephanie Kelly, RN	Belfast	South Eastern Health and Social Care (17)
	Bernardas Valecka, MD	Susan Regan, RN		
		Dawn Turnbull		
	Anoop Chauhan, MD	Catherine Fleming	Blackpool	Blackpool Teaching Hospitals (16)
		Arijit Ghosh		
		Karen Gratrix		
		Stephen Preston		
	Craig Barr, MD	Anne Cartwright	Dudley	Russells Hall Hospital (15)
	Khaled Alfakih, MBBS, MD	Abigail Knighton, BSc., PG Dip.	London	King's College NHS Foundation Hospital (14)
	Jonathan Byrne, PhD	Katherine Martin, RGN, Dip. N, MSc		
	Ian Webb, PhD, MA			
	Peter Henriksen, PhD, MB ChB, BSc(Hons)	Laura Flint, RGN	Edinburgh	Royal Infirmary of Edinburgh (13)
		James Harrison, BSc(Hons), PG dip		
	Peter OKane, MD	Nicki Lakeman	Bourneouth	Royal Bournemouth Hospital (13)
		Anja Ljubez		
	Ramesh de Silva, MB ChB, MD		Bedford	Bedford Hospital NHS Trust (11)
	Dwayne S. G. Conway, MD	Judith Wright	Wakefield	Pinderfields Hospital (11)
		Donna Exley		
	Alexander A Sirker, MB BChir, PhD		London	
		Mervyn Andiapen, RN		University College London Hospitals NHS Foundation Trust
		Amy J. Richards, BSc		BartsHealth NHS Trust
				BartsHealth NHS Trust (11)
	Stephen P. Hoole, MD	Lisa Wong, MSc	Cambridge	Papworth Hospital (10)
	Fraser N. Witherow, MD	Melanie J. Munro, RGN	Dorchester	Dorset County Hospital (8)
	Nicola Johnston, MB, Bch BAO, MRCP, MD		Belfast	Belfast Trust (7)
	Mark Harbinson, MB, Bch BAO, MRCP, MD	Michelle McEvoy, RN		
	Simon Walsh, MB, Bch BAO, MD	Caroline Brown, RN		
	Hanna Douglas, MB, Bch BAO, MRCP, MD			
	Matthew Luckie, MD	Thabitha Charles	Manchester	Central Manchester University Hospital (7)
		Laurel Kolakaluri		
		Hannah Phillips		
	Jolanta Sobolewska, MD	Louise Morby, RN	Oldham	The Pennine Acute Hospitals NHS Trust (6)
		Karen Hallett, RN		
		Carolyn Corbett, RN		
		Lynne Winstanley		
	Paramjit Jeetley, MD	Angelique Smit, RN	London	Royal Free London NHS Foundation Trust (6)

(*Continued*)

APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Niket Patel, MD			
	Tushar Kotecha, MBChB, Mpharm			
	Christopher Travill, MBBS, MD	Susan Gent, SRN RGN	Luton	Luton and Dunstable University Hospital NHS FT (5)
	Iqbal Karimullah, MBBS	Nafisa Hussain, BSc		
	Mahmud Al-Bustami, MBBS			
	Denise Braganza, MD	Fiona Haines	Peterborough	Peterborough City Hospital (5)
		Joanne Taaffe		
	Robert Henderson, MD	Jane Burton	Nottingham	Nottingham University Hospitals (4)
	Kate Pointon, MBBS	Maria Colton		
	Surendra Naik, PhD	Rachel King		
	Thomas Mathew, MBBS, MD, DM			
		Ammani Brown, MSc BA RN	Clydebank	University of Glasgow (4)
		Andrew Docherty, RN		
	Colin Berry, BSc MB ChB, PhD	Lisa McCloy, RN		
	Damien Collison, MB ChB	Kate Robb, RN		
	Giles Roditi, MB ChB	Craig Paterson, PhD		
		Wenda Crawford, RN		
		Joanne Kelly, RN		
		Lorraine McGregor, RN		
	Andrew J Moriarty, BSc MB PhD	Anne Mackin, RN, BSc	Craigavon	Cardiovascular Research Unit, Craigavon Area Hospital (2)
	Jason D. Glover, MBBS	Janet P Knight, RN	Basingstoke	Hampshire Hospitals NHS Foundation Trust (2)
	Jiwan Pradhan, MBBS			
	Ghada Mikhail, MD	Tuhina Bose	London	Imperial College Healthcare NHS Trust (1)
	Darrel P. Francis, MD, MA			
Canada (447)*				
Country Leaders				
Vladimir Dzavik, MD				
Shaun Goodman, MD, MSc				
Gilbert Gosselin, MD				
	Gilbert Gosselin, MD	Anna Proietti, RN	Montreal, QC	Montreal Heart Institute (90)
		Myriam Brousseau, RN		
		Magalie Corfias, RN		
		Patricia Blaise		
		Luc Harvey		
	Ariel Diaz, MD		Trois-Rivieres, QC	Centre Hospitalier de Regional Trois-Rivieres (71)
	Philippe Rheault, MD			
	Miguel Barrero, MD			
	Carl-Éric Gagné, MD	Patricia Alarie		

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APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Yanek Pépin-Dubois, MD	Linda Arcand		
	Ricardo Costa, MD	Isabelle Roy		
	Ying Tung Sia, MD	Estelle Montpetit		
	Catherine Lemay, MD			
	Alejandro Gisbert, MD			
	Pierre Gervais, MD			
	Alain Rheault, MD			
		Katia Drouin, RN	Terrebonne, QC	CISSSL-Hopital Pierre-Le Gardeur (42)
	Denis Carl Phaneuf, MD	Christine Bergeron, RN		
	Gilbert Gosselin, MD	Christine Shelley		
		Christine Masson		
	Pallav Garg, MBBS, MSc	Sandy Carr, RN	London, ON	London Health Sciences Centre (35)
		Catherine Bone, RN		
	Benjamin J.W. Chow, MD	Ermina Moga	Ottawa, ON	University of Ottawa Heart Institute (29)
	Renee C. Hessian, MD	Janetta Kourzenkova		
	Rob S. Beanlands, MD	Olga Walter		
	Richard F. Davies, MD			
	Kevin R. Bainey, MD, MSc	Norma Hogg, RN	Edmonton, AB	University of Alberta (28)
		Suzanne Welsh, RN		
	Asim N. Cheema, MD, PhD		Toronto, ON	St. Michael's Hospital (27)
	Akshay Bagai, MD, MHS			
	Ron Wald, MDCM, MPH			
	Shaun Goodman, MD, MSc	Khrystyna Kushniriuk, HBSc, MD		
	John Joseph Graham, MRCP, MB ChB, BSc	Mohammed Hussain		
	Mark Peterson, MD, FRCSC, PhD	Olugbenga Bello		
	Chi-Ming Chow, MD, CM, MSc			
	Beth Abramson, MD, MSc			
	Asim Nazir Cheema, MD	Ishba Syed, MBBS	Mississauga, ON	Dixie Medical Group (24)
	Mohammad Tariq Vakani, MD	Mohammed Hussain, BSc(H)		
		Khrystyna Kushniriuk, MBBS		
	James Cha, MD	Judy Otis, CRC	Oshawa, ON	Dr James Cha (21)
		Rebecca Otis, CRC		
	Andrew G Howarth, MD, PhD	Michelle M Seib, RN	Calgary, AB	University of Calgary (15)
		Sandra M Rivest, RN		
		Rosa Sandonato, BSCN		
	Graham Wong, MD	Jackie Chow	Vancouver, BC	Vancouver General Hospital (15)
		Andrew Starovoytov		
		Naomi Uchida		
		Ngaire Meadows		
	Amar Uxa, MD	Nadia Asif	Toronto, ON	University Health Network (14)

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
		Suzana Tavares		
	Paul Galiwango, MD	Bev Bozek, RN, CCRC	Scarborough, ON	Scarborough Cardiology Research (9)
	Saleem Kassam, MD	Maria Shier		
	Ashok Mukherjee, MD	Lori-Ann Larmand		
	A. Joseph Ricci, MD	Amir Janmohamed		
		Brenda Hart		
	Andy Lam, MD	Jane Marucci	East Grimsby, ON	West Lincoln Memorial Hospital (8)
		Sharon Tai		
	Shamir Mehta, MD	Sonya Brons, RN	Hamilton, ON	Hamilton General Hospital (7)
		Chris Beck, RN		
		Glenda Wong, RN		
		Krystal Etherington		
		Thippeekaa Arumairajah		
	Jacob Udell, MD	Maria Aprile	Toronto, ON	Women's College Hospital (7)
		Sara Karlsson		
		Susan Webber		
	Philippe Généreux, MD	Chantale Mercure	Montréal, QC	Centre Intégré Universitaire de Santé et de Services Sociaux du Montréal (2)
	Adnan Hameed, MD	Nancy Aedy	St. Catharines, ON	Saint Catharines General Hospital (2)
	Ledjalem Daba, MD	Fran Farquharson	Vaughan, ON	Northwest GTA Cardiovascular and Heart Rhythm Program (1)
		Anam Siddiqui		
Brazil (399)				
Country Leaders				
Antonio Carlos Carvalho, MD, PhD				
Renato D. Lopes, MD, PhD				
	Whady Hueb, MD	Myrthes Emy Takiuti, RN	São Paulo	Heart Institute (InCor) University of São Paulo (127)
	Paulo Cury Rezende, MD			
	Expedito Eustáquio Ribeiro Silva, MD			
	Alexandre Ciappina Hueb, MD			
	Paola Emanuela Poggio Smanio, MD, PhD	Leonardo Pizzol Caetano, PhD	São Paulo	Instituto Dante Pazzanese de Cardiologia (98)
	Alexandre Schaan de Quadros, MD		Porto Alegre	Instituto de Cardiologia de Porto Alegre (41)
	Renato Abdala Karam Kalil, MD	Aline Peixoto Deiro		
	José Luiz da Costa Vieira, MD	Alice Manica Muller		
	Gabriel Grossmann, MD	Maria Antonieta Pereira de Moraes		
	Pedro Píccaro de Oliveira, MD	Bruna Maria Ascoli		
	Leonardo Bridi, MD	Sílvia Zottis Poletti		

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Simone Savaris, MD			
	João V Vitola, MD, PhD		Curitiba	Quanta Diagnostico and Terapia (33)
	Rodrigo J Cerci, MD, Msc	Sandra S. Zier, BSc		
	Fabio R Farias, MD, Msc	Vilmar Veiga, Jr, BSc		
	Miguel M Fernandes, MD, PhD			
	José Antonio Marin-Neto, MD, PhD		Ribeirao Preto	Hospital das Clinicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo (31)
	André Schmidt, MD, PhD			
	Moysés de Oliveira Lima Filho, MD, PhD	Diego Franca da Cunha		
	Ricardo Mendes Oliveira, MD			
	João Reynaldo Abbud Chierice, MD			
	Carísi A. Polanczyk, MD	Guilherme G Rucatti, PsyD	Porto Alegre	Hospital de Clínicas de Porto Alegre
	Mariana V. Furtado, MD	Fernanda Igansi, BSc		Hospital de Clínicas de Porto Alegre (12)
	Luis F. Smidt, MD	Mauren P Haeffner, BSc		
	Antonio Carlos Carvalho, MD	Viviane Almeida	Sao Paulo	Unifesp-Hospital São Paulo (9)
	Gustavo Pucci, MD	Gabriela Sanchez de Souza		
	Flavio Lyra, MD			
	Alvaro Rabelo Alves Junior, MD	Mayana Almeida	Salvador	Fundacao Bahiana de Cardilogia (9)
		Viviane dos Santos		
	Marianna D. A. Dracoulakis, MD, PhD	Natalia S Oliveira, RN	Salvador	Hospital da Bahia (8)
	Rodolfo G. S. D Lima, MD			
	Estevao Figueiredo, MD	Bruna Edilena Paulino Azevedo	Belo Horizonte	Hospital Lifecenter (8)
	Paulo Ricardo Caramori, MD	Marco Bizzaro Santos	Porto Alegre	Hospital Sao Lucas da Pontificia Universidade Catolica do Rio Grande do Sol (7)
		Amanda Germann		
		Vitor Gomes		
		Rosa Homem		
		Ellen Magedanz		
	Rogerio Tumelero, MD	Rosane Laimer	Fundo	Hospital Sao Vicente de Paulo (5)
		Alexandre Tognon		
	Frederico Dall'Orto, MD		Pocos de Caldas	Hospital Maternidade e Pronto Socorro Santa Lucia (4)
	Claudio T. Mesquita, MD	Roberta P Santos, RN	Botafogo	Hospital Pró-Cardíaco (3)
	Alexandre S. Colafranseschi, MD			
	Amarino C. Oliveira Jr., MD			
	Luiz A. Carvalho, MD			
	Isabella C. Palazzo, MD			
	Andre S. Sousa, MD			
	Expedito Eustáquio Ribeiro da Silva, MD, PhD		São Paulo	Hospital TotalCor (2)

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Pedro Gabriel Melo de Barros e Silva, MD, PhD	Mariana Yumi Okada, RN		
	Luciana de Pádua Silva Baptista, MD, PhD	Ana Paula Batista, RN		
	Marcelo Jamus Rodrigues, MD	Aline Nogueira Rabaça, BS		
	Marcos Valério Coimbra de Resende, MD, PhD			
	Jose Francisco Saraiva, MD	Larissa Miranda Trama	Sao Paulo	Hospital Celso Pierro (1)
		Talita Silva		
		Camila Thais de Souza Ormundo		
		Carla Vicente		
	Costantino Costantini, MD, PhD	Caroline Pinheiro	Curitiba	Hospital Cardiologico Costantini (1)
		Daniele Komar		
Poland (333)				
Country Leaders				
Witold Ruzyllo, MD				
Hanna Szwed, MD, PhD				
Country Coordinator				
Radoslaw Pracon, MD, PhD				
	Marcin Demkow, MD, PhD		Warsaw	Coronary and Structural Heart Diseases Department, Institute of Cardiology (127)
	Radoslaw Pracon, MD, PhD			
	Cezary Kepka, MD PhD			
	Anna Teresinska, MD PhD	Olga Walesiak		
	Karolina Kryczka, MD PhD	Katarzyna Malinowska		
	Jan Henzel, MD PhD			
	Mateusz Solecki, MD PhD			
	Edyta Kaczmarska, MD PhD			
	Tomasz Mazurek, MD, PhD	Jakub Maksym, MD	Warszawa	Medical University of Warsaw (48)
		Karolina Wojtera, MD		
		Anna Fojt, MD		
		Ewa Szczerba, MD		
	Jaroslaw Drozdz, PhD		Lodz	Cardiology Clinic, Medical University in Lodz (43)
	Bartosz Czarniak, MD			
	Malgorzata Frach (formerly Stasiak), MD			
	Konrad Szymczyk, MD			
	Iwona Niedzwiecka, MD			
	Sebastian Sobczak, MD			
	Tomasz Ciurus, MD			
	Piotr Jakubowski, MD			
	Magdalena Misztal-Teodorczyk, MD			
	Dawid Teodorczyk, MD	Marta Swiderek, MA		
	Aleksandra Fratczak, MD	Ewelina Wojtala, MA		

(*Continued*)

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Marcin Szkopiak, MD			
	Patrycja Lebioda, MD			
	Michal Wlodarczyk, MD			
	Anna Plachcinska, MD			
	Jacek Kusmierek, MD			
	Magdalena Miller, MD			
	Halina Marciniak, MD			
	Karolina Wojtczak-Soska, MD			
	Katarzyna Łuczak, MD			
	Tomasz Tarchalski, MD			
	Anna Cichocka-Radwan, MD			
	Hanna Szwed, MD, PhD	Jaroslaw Karwowski, MD	Warsaw	National Institute of Cardiology, Warsaw (35)
	Grazyna Anna Szulczyk, MD			
	Adam Witkowski, MD, PhD		Warsaw	Department of Interventional Cardiology and Angiology, Institute of Cardiology (20)
	Krzysztof Kukuła, MD, PhD			
	Małgorzta Celińska-Spodar, MD			
	Joanna Zalewska, MD			
	Grzegorz Gajos, MD, PhD		Krakow	Department of Coronary Disease, John Paul II Hospital, Jagiellonian University Medical College (16)
	Krzysztof Bury, MD, PhD			
	Piotr Pruszczyk, MD, PhD	Andrzej Łabyk, MD	Warszawa	Department of Internal Medicine and Cardiology, Infant Jesus Teaching Hospital, Medical University of Warsaw (15)
	Marek Roik, MD, PhD	Agnieszka Szramowska, MD		
		Olga Zdończyk, MD		
	Krystyna Łoboz-Grudzień, MD, PhD	Joanna Jaroch, MD, PhD	Wrocław	T.Marciniak Hospital (11)
	Leszek Sokalski, MD, PhD			
	Barbara Brzezińska, MD, PhD			
	Maciej Lesiak, Professor, MD		Poznan	Szpital Kliniczny Przemienienia Pańskiego (10)
	Magdalena Łanocha, MD			
	Krzysztof W. Reczuch, MD	Adam Kolodziej, MD	Wroclaw	Military Hospital/Medical University (4)
	Zbigniew Kalarus, MD		Zabrze	Medical University of Silesia, School of Medicine with the Division of Dentistry, Department of Cardiology, Congenital Heart Diseases and Electrotherapy, Silesian Center for Heart Diseases (3)
	Andrzej Swiatkowski, MD			

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Mariola Szulik, MD			
	Wlodzimierz J. Musial, MD	Marta Marcinkiewicz-Siemion, MD	Bialystok	University Hospital in Bialystok (1)
Russia (303)				
Country Coordinator				
Olga Bockeria, MD, PhD				
	Leo Bockeria, MD, PhD	Olga Bockeria, MD, PhD	Moscow	National Medical Research Center for Cardiovascuar Surgery (113)
	Karen Petrosyan, MD, PhD	Zalina Kudzoeva, MD		
	Tatiana Trifonova, MD	Nodira Aripova, MD		
	Alexander M. Chernyavskiy, MD, PhD	Ivan A. Naryshkin, MD	Novosibirsk	E.Meshalkin National Medical Research Center of the Ministry of Health of the Russian Federation (101)
	Evgeniy I. Kretov, MD	Alena Kuleshova, MD		
	Igor O. Grazhdankin, MD	Dastan Malaev, MD		
	Leonid L. Bershtein, MD, PhD		Saint Petersburg	North-Western State Medical University (50)
	Sergey A. Sayganov, MD, PhD	Irina Subbotina		
	Anastasia M. Kuzmina-Krutetskaya, MD	Victoria Gumerova		
	Elizaveta V. Zbyshevskaya, MD, PhD			
	Nana O. Katamadze, MD, PhD			
	Elena A. Demchenko, MD, PhD	Olga B. Nikolaeva, MD	Saint Petersburg	Federal Almazov North-West Medical Research Centre (39)
	Pavel S. Kozlov, MD			
	Vikentiy Y. Kozulin, MD			
	Ekaterina I. Lubinskaya, MD			
Spain (286)*				
Country Leader				
Jose Luis Lopez-Sendon, MD, PhD				
Country Coordinator				
Almudena Castro, MD				
	Jose Lopez-Sendon, MD, PhD	Virginia Fernández-Figares, Pharm	Madrid	Hospital La Paz. IdiPaz (118)
	Almudena Castro, MD			
	Elena Refoyo Salicio, MD			
	Gabriela Guzman, MD			
	Gabriel Galeote, MD			
	Silvia Valbuena, MD			
	Jesús Peteiro, MD, PhD		A Coruna	Complexo Hospitalario Universitario A Coruña Sergas, Department of Cardiology. INIBIC A Coruña. CIBER-CV. Universidad de A Coruña, Spain (112)
	María Dolores Martínez-Ruíz, MD			
	Ruth Pérez-Fernández, MD	Moisés Blanco-Calvo, PhD		

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	José J Cuenca-Castillo, MD	Encarnación Alonso-Álvarez, BSc		
	Xacobe Flores-Ríos, MD	Paula García-González, BSc		
	Óscar Prada-Delgado, MD			
	Gonzalo Barge-Caballero, MD			
	Jose Ramon Gonzalez Juanatey, MD, PhD	Jose Seijas Amigo, Pharm	Santiago de Compostela	Hospital Clinico Universitario de Santiago (17)
	Miguel Souto Bayarri, MD, PhD			
	Virginia Pubull Nuñez, MD			
	Raymundo Ocaranza Sanchez, MD, PhD			
	Belen Cid Alvarez, MD			
	Carlos Peña Gil, MD, PhD			
	Amparo Martinez Monzonis, MD			
	Alessandro Sionis, MD	Ana Fernández Martínez, RN	Barcelona	Hospital de la Santa Creu i Sant Pau (11)
	Montserrat Vila Perales, MD			
	Josep Maria Padró, MD			
	Antonio Serra Peñaranda, MD			
	Joan García Picart, MD			
	Antonino Ginel Iglesias, MD			
	Xavier Garcia-Moll Marimon, MD			
	Guillem Pons Lladó, MD			
	Francesc Carreras Costa, MD			
	Vicente Miro, MD	Begoña Igual, MD	Valencia	Hospital Universitario y Politecnico La Fe (10)
	Jose L Diez, MD			
	Pilar Calvillo, MD			
	F. Marin Ortuño, MD, PhD		Murcia	HUVA, Hospital Clínico Universitario Virgen De La Arrixaca (8)
	M. Valdés Chávarri, MD, PhD	M. Quintana Giner, MD		
	A. Tello Montolliu, MD, PhD	A.I. Romero Aniorte, MD		
	E. Pinar Bermudez, MD, PhD	JM. Rivera Caravaca, MD		
	G. De La Morena, MD, PhD			
	Montserrat Gracida Blancas, MD	Olga Cañavate	Barcelona	Hospital De Bellvitge (4)
		Sonia Guerrero		
		Silvia Riera		
	Jose Enrique Castillo Luena, MD	Jose Enrique Castillo Luena	Zaragoza	Hospital Universitario Miguel Servet (4)
		Maria Lasala		
	Francisco Fernandez-Aviles, MD	Maria Lorenzo	Madrid	Hospital General Universitario Gregorio Maranon (2)
		Olga Sobrino		
		Alexandra Vazquez		
China (246)				
Country Leader				
Lixin Jiang, MD, PhD				

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Jiyan Chen, MD	Haojian Dong	Guangzhou	Guangdong General Hospital (102)
		Peiyu He		
		Chunli Xia		
		Junqing Yang		
		Qi Zhong		
	Yongjian Wu, MD, PhD	Yanmeng Tian, MD	Beijing	Chinese Academy of Medical Sciences, Fuwai Hospital (17)
		Dongze Li	Urumqi	First Affiliated Hospital of Xinjiang Medical University (15)
	Yitong Ma, MD	Xiaomei Li		
	Yining Yang, MD	Xiang Ma		
		Zixiang Yu		
		Qian Zhao		
	Zheng Ji, MD	Chunguang Li	Tangshan	Tangshan Gongren Hospital (15)
		Lei Zhang		
		Yu Zhao		
		Bolin Zhu		
	Xinchun Yang, MD	Mulei Chen	Beijing	Beijing Chao-yang Hospital, Capital Medical University (12)
		Hongjie Chi		
		Yang Wang		
		Jing Zhang		
	Wenhua Lin, MD	Rui Jing	Tianjing	TEDA International Cardiovascular Hospital (12)
		Jingjing Liu		
	Hesong Zeng, MD	Qiang Zhou, MD	Wuhan	Tongji Medical College (11)
		Chang Xu, MD		
		Zhuxi Li, MD		
		Junhua Li, MD		
		Luyang Xiong, MD		
	Xin Fu, MD	Dan Gao	Zhengzhou	The First Affiliated Hospital of Zhengzhou University (11)
		Dengke Jiang		
		Ran Leng		
		Xutong Wang		
		Qianqian Yuan		
		Lili Zhang		
	Bin Yang, MD	Ziliang Bai	Taiyuan	Shanxi Cardiovascular Hospital (10)
		Jianhua Li		
		Jie Qi		
		Fei Wang		
		Haitao Wang		

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
		Bin Yang		
		Zhou Yue		
		Zhulin Zhang		
	Songtao Wang, MD	Yumei Dong	Qingdao	Qingdao Fuwai Hospital (8)
		Jiajia Mao		
		Bin Zhang		
	Gong Cheng, MD	Xiuhong Li	Xian	Shanxi Provincial People's Hospital (6)
		Xiaowei Yao		
		Nier Zhong		
		Ning Zhou		
	Yulan Zhao, MD	Yaping Huang, MS	Zhengzhou	The Second Affiliated Hospital of Zhengzhou University (6)
		Panpan Zhou, MS		
	Xuehua Fang, MD	Wei Su	Beijing	Liangxiang Hospital, Beijing Fangshan District (6)
	Qiutang Zeng, MD	Yu Kunwu	Wuhan	Wuhan Union Hospital, Tongji Medical College, Huazhong Science and Tech University (3)
		Yudong Peng		
		Xin Su		
	Xi Su, MD	Chen Wang	Wuhan	Wuhan Asia Heart Hospital (3)
		Yunhai Zhao		
	Qingxian Li, MD	Yaming Geng	Jining	Affiliated Hospital of Jining Medical University (3)
		Yanfu Wang		
	Shao-ping Nie, MD, PhD	Jing-yao Fan, MD	Beijing	Beijing Anzhen Hospital (2)
		Si-ting Feng, MD,PhD		
		Xiao Wang, MD,PhD		
		Yan Yan, MD,PhD		
		Hui-min Zhang, MD,PhD		
	Qin Yu, MD	Lingping Chi	Dalian	Affiliated Zhongshan Hospital of Dalian University (2)
		Fang Liu		
	Jian'an Wang, MD	Han Chen	Hangzhou	The Second Affiliated Hospital Zhejiang University School of Medicine (1)
		Jun Jiang		
		Huajun Li		
		Jian'an Wang		
		Yechen Han, MM	Beijing	Peking Union Medical College Hospital (1)
		Lihong Xu, RN		
	Shuyang Zhang, MD, PhD	Zhenyu Liu		

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Zhenyu Liu, MD	Gang Chen		
		Rongrong Hu		
Italy (139)*				
Country Leader				
Aldo P. Maggioni, MD				
	Gian Piero Perna, MD	Francesca Pietrucci, PhD	Ancona	Cardiology and CCU-Ospedali Riuniti Ancona (54)
	Marco Marini, MD			
	Gabriele Gabrielli, MD			
	Stefano Provasoli, MD	Anna Di Donato	Varese	Ospedale di Circolo e Fondazione Macchi (23)
	Edoardo Verna, MD			
	Lorenzo Monti, MD		Rozzano	Humanitas Research Hospital, Rozzano (MI) (17)
	Barbara Nardi, MD			
	Antonio Di Chiara, MD	Francesca Pezzetta, MD	Tolmezzo	Azienda Servizi Sanitaria n.3 Alto Friuli-Collinare-Medio Friuli (9)
	Andrea Mortara, MD	Valentina Casali, MD	Monza	Policlinico di Monza, Monza MB (8)
	Marcello Galvani, MD	Chiara Attanasio	Forli	Ospedale "G.B. Morgagni–L. Pierantoni" Forli (AUSL della Romagna) (8)
	Filippo Ottani, MD			
	Marco Sicuro, MD	Gianpiero Leone, MD	Aosta	Ospedale Regionale Umberto Parini (5)
		Francesco Pisano, MD		
		Cristina Bare, BSc		
	Paolo Calabro, MD	Fabio Fimiani	Napoli	AORN Dei Colli "V. Monaldi" UOC Cardiologia Università della Campania "L.Vanvitelli" (4)
	Tiziana Formisano, MD			
	Giuseppe Tarantini, MD	Alberto Barioli, MD	Padua	University of Padua-Cardiology Clinic (3)
	Umberto Cucchini, MD	Federica Ramani		
	Anto Luigi Andres, MD			
	Emanuela Racca, MD	Fabrizio Rolfo, MD	Cuneo	Azienda Ospedaliera S. Croce e Carle (3)
		Cecilia Goletto		
	Carlo Briguori, MD	Francesca De Micco	Naples	Clinica Mediterranea (2)
	Roberto Amati, MD	Stefano Di Marco, MD	Pescia	UO Cardiologia Ospedale SS Cosma e Damiano (2)
	William Vergoni, MD	Martina Tricoli		
	Aldo Russo, MD	Massimo Villella, MD	San Giovanni Rotondo	IRCCS "Casa Sollievo della Sofferenza" (1)
	Raffaele Fanelli, MD			
Singapore (61)*				
Country Leader				

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
Harvey Douglas White, MD				
Country Coordinator				
Caroline Alsweiler				
	Kian-Keong Poh, MD		Singapore	National University Heart Center Singapore (33)
	Ping Chai, MD			
	Titus Lau, MD			
	Joshua P. Loh, MD			
	Edgar L. Tay, MD			
	Kristine Teoh, MD	Sik-Yin V Tan, BSc		
	Lynette L. Teo, MD	Winnie C Sia, BSc		
	Ching-Ching Ong, MD	Audrey W Leong, BSc		
	Raymond C. Wong, MD			
	Poay-Huan Loh, MD			
	Theodoros Kofidis, MD			
	Wan Xian Chan, MD			
	Koo Hui Chan, MD			
	David Foo, MBBS	Li Hai Yan, RN	Singapore	Tan Tock Seng Hospital (22)
	Jason Loh Kwok Kong, MD			
	Ching Min Er, MD			
	Fahim Haider Jafary, MD			
	Terrance Chua, MD	Nasrul Ismail	Singapore	National Heart Centre Singapore (6)
		Min Tun Kyaw		
		Deborah Yip		
Germany (54)				
Country Leader				
Rolf Doerr, MD				
	Rolf Doerr, MD		Dresden	Praxisklinik Herz und Gefaesse (29)
	Juergen Stumpf, MD	Dorit Grahl		
	Klaus Matschke, MD, PhD	Franziska Guenther		
	Gregor Simonis, MD, PhD	Kerstin Bonin		
	Clemens T. Kadalie, MD			
	Udo Sechtem, MD	Ina Wenzelburger	Stuttgart	Robert-Bosch-Krankenhaus (22)
	Peter Ong, MD	Susanne Gruensfelder, RN		
	P. Christian Schulze, MD, PhD		Jena	University Hospital Jena (2)
	Bjoern Goebel, MD			
	Karsten Lenk, MD			
	Georg Nickenig, MD	Jan-Malte Sinning, MD	Bonn	Universitatsklinikum Bonn (1)
		Marcel Weber, MD		
		Nikos Werner, MD		
Austria (50)				
Country Leaders				

(*Continued*)

APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
Irene Marthe Lang, MD				
Kurt Huber, MD				
	Herwig Schuchlenz, MD	Gudrun Steinmaurer	Graz	LKH Graz West Austria (35)
	Stefan Weikl, MD			
	Irene Marthe Lang, MD	Max-Paul Winter, MD	Vienna	Medical University of Vienna, Department of Cardiology (8)
		Tijana, Andric, MD	Vienna	Wilhelminen Hospital Vienna (7)
	Kurt Huber, MD	Maximilian, Tscharre, MD		
	Gabriele, Jakl-Kotauschek, MD	Claudia, Wegmayr, MSc		
		Bernhard, Jäger, MD		
		Florian, Egger, MD		
Hungary (49)				
Country Leader				
Matyas Keltai, MD, PhD, DSc				
	Andras Vertes, MD	Judit Sebo, MD	Budapest	Eszszk- Szent Istvan Hospital (20)
		Zoltan Davidovits, MD		
		Laszlone Matics		
	Albert Varga, MD, PhD	Gergely Ágoston, MD	Szeged	University of Szeged (12)
	Geza Fontos, MD	Gabor Dekany, MD	Budapest	George Gottsegen National Institute of Cardiology (9)
	Bela Merkely, MD, PhD, DSc	Andrea Bartykowszki, MD	Budapest	Heart and Vascular Center, Semmelweis University (8)
		Pal Maurovich-Horvat, MD, PhD, MPH		
	Gabor Kerecsen, MD	Agnes Jakal	Budapest	Military Hospital, Budapest (1)
Serbia (47)				
	Sasa Hinic, MD, BSc	Jelena Djokic, MD	Belgrade	University Hospital Center Bezanijska Kosa (13)
	Marija Zdravkovic, MD, PhD			
	Vladan Mudrenovic, MD			
	Bogdan Crnokrak, MD			
	Branko D. Beleslin, MD, PhD		Belgrade	Faculty of Medicine, University of Belgrade; Cardiology Clinic, Clinical Center of Serbia (10)
	Nikola N. Boskovic, MD	Ana D. Djordjevic-Dikic, MD, PhD		
	Marija T. Petrovic, MD	Vojislav L. Giga, MD, PhD		
	Milan R. Dobric, MD	Jelena J. Stepanovic, MD, PhD		
	Zeljko Z. Markovic, MD, PhD			
	Ana S. Mladenovic, MD, PhD			

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APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Nada Cemerlic-Adjic, MD	Lazar Velicki, MD	Sremska Kamenica	Institute of Cardiovascular Diseases Vojvodina, Sremska Kamenica, Serbia and Faculty of Medicine, University of Novi Sad (9)
		Ljiljana Pupic		
	Goran Davidović, MD, PhD	Stefan M. Simović, MD	Kragujevac	Clinical Center Kragujevac (7)
	Rada Vučić, MD			
	Milica Nikola Dekleva, MD PhD	Miroslav Stevo Martinovic, MD	Belgrade	University Clinical Hospital Zvezdara (6)
		Gordana Stevanovic		
	Goran Stankovic, MD	Milan Dobric	Belgrade	Clinical Center of Serbia (1)
	Svetlana Apostolovic, MD	Sonja Salinger Martinovic	Nis	Clinic for Cardiovascular Diseases, Clinical Center Nis (1)
		Dragana Stanojevic		
Mexico (46)				
	Jorge Escobedo, MD	Ramon de Jesús-Pérez, RN	Benito Juarez	Instituto Mexicano del Seguro Social (35)
	Rubén Baleón-Espinosa, MD			
	Arturo S Campos-Santaolalla, MD			
	Elihú Durán-Cortés, MD			
	José M Flores-Palacios, MD			
	Andrés García-Rincón, MD			
	Moisés Jiménez-Santos, MD			
	Joaquín V Peñafiel, MD			
	José A Ortega-Ramírez, MD			
	Aquiles Valdespino-Estrada, MD			
	Erick Alexánderson Rosas, MD	María Fernanda Canales Brassetti, MD	Mexico City	Instituto Nacional de Cardiología "Ignacio Chávez" (11)
		Diego Adrián Vences Anaya, MD		
		María Pérez García		
		Isabel Estela Carvajal Juarez, MD		
		Magdalena Madero Rovalo, MC		
		Erick Donato Morales Rodríguez, MD		
Australia (45)				
Country Leaders				
Joseph B. Selvanayagam, MBBS (Hons), DPhil				
Jamie Rankin, MBBS *(past)*				
Country Coordinator				
Deirdre Murphy				
	Joseph B. Selvanayagam, MBBS (Hons), DPhil	Sau Lee, PhD	Adelaide	Flinders Medical Centre (30)
	Majo X. Joseph, MBBS	Prince Thomas, RN		

(*Continued*)

APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Suku T. Thambar, MBBS	Melissa D Chaplin, RN	New Lambton Heights	John Hunter Hospital (8)
		Stephanie C Boer, B Biotechnology (Honors)		
	John F. Beltrame, MD	Jeanette K. Stansborough, RN	Woodville South	The Queen Elizabeth Hospital (5)
		Marilyn Black, RN		
	Graham S. Hillis, PhD	Michelle M. Bonner, B. Nursing	Perth	Royal Perth Hospital (2)
		Kim F. Ireland, RN		
		Clare Venn-Edmonds, RN		
France (42)				
Country Leader				
Philippe-Gabriel Steg, MD				
Country Coordinators				
Helene Abergel				
Jean-Michel Juliard				
		Corine Thobois, RN	Chartres	C.H. Louis Pasteur (21)
	Christophe Thuaire, MD	Emilie Tachot, RN		
	Téodora Dutoiu, MD	Christophe Laure, RN		
		Christel Vassaliere, RN		
	Philippe Gabriel Steg, MD	Helene Abergel, MSc	Paris	Bichat Hospital (9)
	Jean-Michel Juliard, MD	Axelle Fuentes, MSc		
	Michel S. Slama, MD	Ludivine Eliahou, MD	Clamart Cedex	Antoine-Beclere Hospital (5)
	Rami El Mahmoud, MD	Olivier Dubourg, MD	Boulogne	Ambroise Pare Hospital (2)
		Pierre Michaud, MD		
	Eric Nicollet, MD	Sarah Hadjih	Corbeil-Essonnes Cedex	Centre Hospitalier Sud Francilien (2)
	Pascal Goube, MD	Patricia Brito		
	Gilles Barone-Rochette, MD	Gilles Barone-Rochette	Grenoble	Grenoble University Hospital (2)
	Alain Furber, MD	Charles Cornet, MD, PhD	Angers Cedex 9	Centre Hospitalier Universitaire d'Angers (1)
	Loïc Bière, MD	Jeremy Rautureau, MD, PhD		
Lithuania (39)				
		Agne Juceviciene, MD	Vilnius	Vilnius University Hospital Santariskes Clinic (39)
		Irma Kalibataite-Rutkauskiene, MD		
		Laura Keinaite		
	Aleksandras Laucevicius, MD	Monika Laukyte		
	Jelena Celutkiene, MD	Gelmina Mikolaitiene		
		Akvile Smigelskaite, MD		
		Ilona Tamasauskiene, MD		
		Agne Urboniene, MD		
Netherlands (37)*				
	Elvin Kedhi MD, PhD		Zwolle	Isala Klinieken (25)
	Jorik Timmer, MD	Ilse Bouwhuis		

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Rik Hermanides, MD	Lia Nijmeijer		
	Eliza Kaplan, MD			
	Robert K. Riezebos, MD, PhD		Amsterdam	Cardio Research Hartcentrum OLVG (11)
	Pouneh Samadi, MD	Jeannette, J. M. Schoep, RN		
	Elise van Dongen, MD	Elisabeth, M. Janzen, RN		
	Sander R. Niehe, MD			
	Harry Suryapranata, MD	Sandra Ahoud	Nijmegen	Radboudumc (1)
	Stijn van Vugt, MD, PhD			
Portugal (33)				
	Ruben Ramos, MD		Lisbon	Hospital de Santa Marta (25)
	Duarte Cacela, MD			
	Ana Santana, MD			
	Antonio Fiarresga, MD			
	Lidia Sousa, MD			
	Hugo Marques, MD			
	Lino Patricio, MD	Mafalda Selas		
	Luis Bernanrdes, MD	Filipa Silva		
	Pedro Rio, MD	Cláudia Freixo		
	Ramiro Carvalho, MD			
	Rui Ferreira, MD			
	Tiago Silva, MD			
	Ines Rodrigues, MD			
	Pedro Modas, MD			
	Guilherme Portugal, MD			
	Jose Fragata, MD			
	Fausto J. Pinto, PhD	Inês Zimbarra Cabrita, PhD	Lisbon	Santa Maria University Hospital, Cardiology Department, CHLN (6)
	Miguel Nobre Menezes, MD	Andreia Rocha, MSc		
	Guilhermina Cantinho Lopes, MD	Francisca Patuleia Figueiras, PhD		
	Ana Gomes Almeida, PhD	Andreia Coelho, BSc		
	Pedro Canas Silva, MD	Marta Capinha		
	Angelo Nobre, MD	Maria Inês Caetano		
	Ana Rita Francisco, MD	Susana Silva		
	Nuno Ferreira, MD		Vila Nova de Gaia	Centro Hospitalar de Vila Nova de Gaia/Espinho, EPE (2)
	Ricardo L. Lopes, MD			
Argentina (29)				
Country Leader				
Rafael Diaz, MD *(past)*				
	Luis Guzman, MD	Veronica Tinnirello	Cordoba	Instituto Medico DAMIC (11)
	Julio César Figal, MD	Matías Nicolás Mungo	Ciudad Autonoma de Buenos Aires	Fundación Favaloro (10)
	Oscar Méndiz, MD			

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APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Claudia Cortés, MD			
	Roberto René Favaloro, MD			
	Carlos Alvarez, MD	Marina Garcia	Bahia Blanca	Hospital Italiano Regional del Sur Bahia Blanca (3)
	Javier Courtis, MD	Valeria Godoy	Cordoba	Clinica Romagosa and Clinica De La Familia (2)
	Gabriela Zeballos, MD			
	Lilia Schiavi, MD	Maria Victoria Actis	Cordoba	Clinica Del Prado (2)
	Mariano Rubio, MD	Graciela Scaro, MD	Cordoba	Clínica Privada Vélez Sarsfield (1)
New Zealand (28)*				
Country Leader				
Harvey Douglas White, MD				
Country Coordinator				
Caroline Alsweiler				
	Gerard Patrick Devlin, MD	Liz Low, RN	Hamilton	Waikato Hospital (22)
	Raewyn Fisher, MD	Jayne Scales, RN		
		Kirsty Abercrombie, RN		
	Ralph Alan Huston Stewart, MCChB, MD	Leah Howell, RN	Auckland	Auckland City Hospital (6)
	Harvey Douglas White, MD	Cathrine Patten, RN		
	Jocelyne Benatar, MD			
Macedonia (28)*				
	Sasko Kedev, MD, PhD		Skopje	University Clinic of Cardiology (28)
	Irena Peovska Mitevska, MD, PhD			
	Elizabeta Srbinovska Kostovska, MD, PhD			
	Hristo Pejkov, MD, PhD			
Sweden (23)*				
Country Leader				
Claes Held, MD, PhD				
	Claes Held, MD, PhD		Uppsala	Uppsala University (18)
	Kai Eggers, MD, PhD			
	Gunnar Frostfelt, MD, PhD	Christina Björklund, RN		
	Nina Johnston, MD, PhD	Maria Andreasson, RN		
	Maciej Olsowka, MD	Marie Essermark, RN		
	Axel Åkerblom, MD, PhD			
	Inga Soveri, MD, PhD			
	Johannes Aspberg, MD	Liselotte Persson	Stockholm	Karolinska Institutet at Danderyd Hospital (5)
Israel (15)				
Country Leaders				
Rafael Beyar, MD, MD, DSc, MPH				
Tali Sharir, MD				
Country Coordinator				
Eugenia Nikolsky, MD				
	Tali Sharir, MD	Or Harel, MA	Tel-Aviv	Assuta Medical Centers (9)

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APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Dan Elian, MD			
	Arthur Kerner, MD	Margalit Bentzvi	Haifa	Rambam Medical Center (6)
	Samia Massalha, MD	Ludmila Helmer		
Japan (14)				
Country Leader				
Shun Kohsaka, MD				
	Keiichi Fukuda, MD, PhD	Ikuko Ueda, PhD	Shinjuku-ku	Keio University (7)
	Shun Kohsaka, MD	Jun Fujita, MD		
	Satoshi Yasuda, MD, PhD	Akemi Furukawa, RN	Suita-shi	National Cerebral and Cardiovascular Center
		Kanae Hirase, RN		National Cerebral and Cardiovascular Center (4)
		Toshiyuki Nagai, MD, PhD		
		Fumiyuki Otsuka, MD, PhD		
	Shigeyuki Nishimura, MD	Shintaro Nakano	Hidaka	Saitama Medical University (3)
Belgium (7)*				
Country Leader				
Frans Van de Werf, MD, PhD				
Country Coordinator				
Kaatje Goetschalckx, MD				
	Kaatje Goetschalckx, MD	Valerie Robesyn	Leuven	University Hospital Leuven (7)
	Frans Van de Werf, PhD, MD			
	Kathleen Claes, PhD, MD			
Taiwan (7)*				
Country Leader				
Harvey Douglas White, MD				
Country Coordinator				
Caroline Alsweiler				
	Chung-Lieh Hung, MD	Yi-Hsuan Yang	Taipei City	Mackay Memorial Hospital (7)
	Chun-Ho Yun, MD			
	Charles Jia-Yin Hou, MD			
	Jen-Yuan Kuo, MD			
	Hung-I Yeh, MD, PhD			
	Ta-Chuan Hung, MD			
	Jiun-Yi Li, MD, PhD			
	Chen-Yen Chien, MD, PhD			
	Cheng-Ting Tsai, MD			
	Chun-Chieh Liu, MD			
	Fa-Chang Yu, MD			
	Yueh-Hung Lin, MD			
	Wei-Ren Lan, MD			
	Chih-Hsuan Yen, MD			
	Jui-Peng Tsai, MD			

(*Continued*)

APPENDIX Continued

Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Kuo-Tzu Sung, MD			
South Africa (7)*				
	Mpiko Ntsekhe, MD		Cape Town	Groote Schuur Hospital/ University of Cape Town (7)
	Shaheen Pandie, MD	Constance Philander (Nee Talliard), ND		
	Charle A Viljoen, MD	Noloyiso Mtana, RN		
	Marianne De Andrade, MD			
Switzerland (7)*				
Country Leader				
Aldo P. Maggioni, MD				
	Tiziano Moccetti, MD	Adriana Anesini, RN	Lugano	Cardiocentro (7)
	M.Grazia Rossi, MD	Simona Maspoli, RN		
		Manuela Mombelli, RN		
Egypt (6)				
	Magdy Abdelhamid, MD	Ahmed Talaat, MD	Cairo	Cairo University (6)
	Ahmed Adel, MD			
	Ahmed Kamal, MsC			
	Hossam Mahrous, MD			
	Sameh El Kaffas, MD			
	Hussien El Fishawy, MD			
Romania (5)				
	Calin Pop, MD, PhD		Bucharest	Emergency County Hospital Baia Mare (4)
	Matei Claudia, MD, PhD			
	Bogdan A. Popescu, MD, PhD		Bucharest	Emergency Institute of Cardiovascular Diseases "Prof. Dr C. C. Iliescu" (1)
	Carmen Ginghina, MD, PhD	Monica Rosca, MD, PhD		
	Dan Deleanu, MD, PhD	Carmen C. Beladan, MD, PhD		
	Vlad A. Iliescu, MD, PhD			
Saudi Arabia (5)*				
	Mouaz H. Al-Mallah, MD MSc	Sarah Zahrani, RN	Central Province	King AbdulAziz Cardiac Center (5)
	Ahmed Aljzeeri, MD			
	Hani Najm, MD			
	Ali Alghamdi, MD			
Peru (4)*				
	Walter Enrique Mogrovejo Ramos, MD	Marco Antonio Monsalve Davila, RN	Mirafloes	Instituto Neuro Cardiovascular De Las Americas (4)
Thailand (3)				
Country Leader				
Harvey Douglas White, MD				
Country Coordinator				
Caroline Alsweiler				
	Srun Kuanprasert, MD		Chiang Mai	Maharaj Nakorn Chiang Mai Hospital (2)
	Arintaya Prommintikul, MD			

(*Continued*)

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Country (No. Randomizations)	Investigator(s)	Study Coordinator(s)	City and State	Institution (No. Randomizations)
	Weerachai Nawarawong, MD	Supatchara Khwakhong, RN		
	Surin Woragidpoonpol, MD	Anong Chaiyasri, RN		
	Thitipong Tepsuwan, MD	Warangkana Mekara, RN		
	Noppon Taksaudom, MD	Supap Kulthawong, RN		
	Chataroon Rimsukcharoenchai, MD	Anong Amaritakomol, RN		
	Juntima Euathrongchit, MD			
	Yutthaphan Wannasopha, MD			
	Sukit Yamwong, MD	Pachara Panpunuan, RN	Bangkok	Ramathibodi Hospital (1)
	Piyamitr Sritara, MD			
	Suthara Aramcharoen, MD			
	Krissada Meemuk, MD			
Malaysia (2)*				
Country Leader				
Harvey Douglas White, MD				
Country Coordinator				
Caroline Alsweiler				
	Ahmad Khairuddin, MD	Noor Syamira Mokhtar, RN	Kuala Lumpur	Institut Jantung Negara (2)
	Hafidz Abd Hadi, MD	Nor Asiah Basri, RN		
	Shaiful Azmi Yahaya, MD	Irni Yusnida, RN		
		Humayrah Hashim		

*Countries participated in Economics Quality of Life Questionnaires.

† This site received 1 participant in transfer who was randomized at another site.

NHS, National Health Service; NIH, National Institutes of Health; PI, Primary Investigator; UAB, University of Alabama Birmingham; VA, Veterans Affairs; VAMC, Veterans Affairs Medical Center.

ARTICLE INFORMATION

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Affiliations

NYU Grossman School of Medicine, New York, NY (H.R.R., S.B., J.D.N., J.S.B., J.S.H.); Duke Clinical Research Institute, Durham, NC (D.D.C., K.P.A., R.D.L., S.M.O.); Cedars-Sinai Smidt Heart Institute, Los Angeles, CA (C.N.M.); Icahn School of Medicine at Mount Sinai, Cardiovascular Research Foundation, New York, NY (L.J.S., G.W.S.); St. Louis University School of Medicine, St. Louis, MO (B.R.C.); VA New England Healthcare System, Bedford, MA (W.E.B.); National Heart, Lung, and Blood Institute, Bethesda, MD (Y.D.R.); Dept of Medical Sciences, Cardiology, Uppsala University and Uppsala Clinical Research Center, Uppsala, Sweden (C.H.); Saint Luke's Mid America Heart Institute/University of Missouri - Kansas City (UMKC), Kansas City, MO (J.S.); Department of Cardiovascular Diseases, UZ Leuven, Leuven, Belgium (K.G.); National Research Center for Cardiovascular Surgery, Moscow, Russia (O.B.); Northwick Park Hospital-Royal Brompton Hospital, London, United Kingdom (A.E.); Cleerly Inc., New York, NY (J.K.M.); Cedars-Sinai Medical Center, Los Angeles, CA (D.S.B.); Massachusetts General Hospital and Harvard Medical School, Boston, MA (M.H.P.); Brigham and Women's Hospital, Boston, MA (R.Y.K.); Department of Medicine, Stanford University School of Medicine, Stanford, CA (R.A.H., D.J.M.); and Hospital Cruz Vermelha Portuguesa, Lisbon, Portugal (B.T.).

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Supplemental Material

Data S1
Tables S1–S6
Figure S1–S2
Reference [39]

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