

SUPPLEMENTAL MATERIAL

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Supplement Section I: Quality of Life Instruments Collected in the ISCHEMIA Trial and Comprehensive QOL Substudy

Assessment	Instruments	Constructs Measured
Baseline Assessment	Seattle Angina Questionnaire (19-item) Rose Dyspnea Scale EQ-5D-3L EQ-5D VAS Duke Activity Status Index RAND General Health rating Patient Health Questionnaire-8 Perceived Stress Scale-4 Life Orientation Test-Revised	Angina-related health status Dyspnea General health status General health status Functional capacity General health status Depressive symptoms Perception of stress Optimism
Comprehensive Quality of Life Substudy North America (administered at 3, 12, 24, and 36 months following randomization, and at study close-out) Collected by Duke Clinical Research Institute Outcomes Call Center	Seattle Angina Questionnaire (19-item) Rose Dyspnea Scale EQ-5D-3L EQ-5D VAS Duke Activity Status Index RAND General Health rating Patient Health Questionnaire-8 Perceived Stress Scale-4 Life Orientation Test-Revised	Angina-related health status Dyspnea General health status General health status Functional capacity General health status Depressive symptoms Perception of stress Optimism
Comprehensive Quality of Life Substudy International (administered at 3, 12, 24, and 36 months following randomization, and at study close-out) Collected by site coordinators and recorded on the CRF	Seattle Angina Questionnaire (19-item) Rose Dyspnea Scale EQ-5D-3L EQ-5D VAS Patient Health Questionnaire-8	Angina-related health status Dyspnea General health status General health status Depressive symptoms
Quality of Life Study (administered at baseline and at 1.5, 3 and 6 months and then every 6 months thereafter until study termination) Collected by site coordinators and recorded on the CRF	Seattle Angina Questionnaire-7 (7-item) Rose Dyspnea Scale EQ-5D VAS	Angina-related health status Dyspnea General health status

Quality of Life Instruments Collected in ISCHEMIA

Seattle Angina Questionnaire-19

The Seattle Angina Questionnaire (SAQ) is a validated 19-item CAD-specific health status instrument that assesses patients' function, symptoms, and quality of life over the past 4 weeks.¹ The SAQ quantifies five domains: Physical Limitation (9 items), Angina Stability (1 item), Angina Frequency (2 items), Treatment Satisfaction (4 items) and Quality of Life (3 items). Scores are calculated for each domain. In addition, a summary score is calculated that integrates the Physical Limitation, Angina Frequency, and Quality of Life scores. All scores are scaled 0-100 such that 0 represents the worst possible health status and 100 the

highest. For SAQ scales, 5 or more points represent a benchmark for a clinically significant change for an individual patient.¹

SAQ Angina Frequency (AF) scores interpretive aids have been proposed: daily (SAQ AF score 0-30), weekly (scores of 31-60), monthly (scores of 61-99), and no angina over the past 4 weeks (SAQ AF scores = 100).² SAQ AF asks patients to provide a mental average assessment of events in the preceding 4 weeks, which may vary according to a number of factors (e.g. physical activity) and recall. Thus, terms used to describe SAQ AF score ranges, such as daily, weekly, monthly, or none should be understood to reflect descriptive approximations rather than precise categories.

EQ-5D-3L

The EuroQOL-5D (EQ-5D) is a commonly used assessment of generic health status consisting of two components. The first component is a descriptive system of five items that assesses different dimensions of health status (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). The version used in ISCHEMIA (EQ-5D-3L) includes three response options for each item. Combinations of responses to these items define different possible health states, which are then mapped to country-specific preference weights, thus reflecting societal valuations of the health states. The second component is a visual analog scale (VAS) that assesses the patient's own valuation of their health, ranging from "best imaginable health state" (100) to "worst imaginable health state" (0).³

Duke Activity Status Index

The Duke Activity Status Index (DASI) is a validated 12-item questionnaire that assesses functional capacity in daily activities for patients with cardiovascular disease. Positive responses are weighted based on metabolic cost (MET) and summed to obtain a score ranging from 0 to 58.2; higher scores denote greater functional capacity.⁴ A clinically meaningful change in the DASI is 4 points or more.⁵

Patient Health Questionnaire-8

The Patient Health Questionnaire-8 (PHQ-8) is an 8-item scale that assesses depressive symptoms.⁶ A single integer summary score is calculated ranging from 0 to 24, with higher scores indicating greater severity of symptoms. A score of 10 or greater is considered major depression, 20 or more is severe major depression.

RAND General Health Rating

The RAND General Health rating is the first item from the RAND 36-Item Health Survey 1.0, which evaluates overall health on an ordinal 5-level scale.⁷ Responses are scored 0 (poor) to 100 (excellent).

Rose Dyspnea Scale

The Rose Dyspnea Scale (RDS) consists of 4 items that assess activities of differing intensity that precipitate dyspnea symptoms.⁸ Scores range from 0 to 4, where 0 indicates no dyspnea with activity and 4 indicates significant limitations due to dyspnea. The minimal clinically important difference for the RDS has not been formally established, although movement of 1 point has been proposed, given that there are only 5 possible values.

Perceived Stress Scale-4

The Perceived Stress Scale-4 (PSS-4) is a 4-item scale that assesses the degree to which the patient views situations in their life as stressful.^{9, 10} A single integer summary score is calculated ranging from 0 to 16, with higher values denoting greater perceptions of stress.

Life Orientation Test-Revised

The Life Orientation Test-Revised (LOT-R) is a 10-item questionnaire that evaluates generalized optimism versus pessimism (4 of the 10 items are "filler" items that are not scored and were not included in the

assessments in ISCHEMIA).¹¹ A single integer summary score is calculated ranging from 0 to 24, with higher scores denoting greater optimism. Scores 0-13 indicate low optimism, 14-18 indicate moderate optimism, and 19-24 indicate high optimism.

Supplement Section II: Supplemental Tables and Figures

Supplement Table 1: Baseline Characteristics in the ISCHEMIA Comprehensive QOL Substudy by Treatment Group, North American Patients*

Patient Characteristics	Invasive Strategy (N=616)	Conservative Strategy (N=618)	p-value
Age at randomization - years	66.5 ± 8.8	66.0 ± 8.6	0.24
Male sex – no.(%)	501/616 (81.3%)	496/618 (80.3%)	0.63
White race† – no./total no. (%)	518/610 (84.9%)	493/608 (81.1%)	0.22
Hypertension – no.(%)	504 (82.0%)	490 (79.3%)	0.24
Diabetes – no.(%)	266 (43.2%)	256 (41.4%)	0.53
Previous myocardial infarction – no.(%)	120 (19.6%)	121 (19.7%)	0.95
New onset of angina over the past 3 months – no./total (%)	95/546 (17.4%)	99/552 (17.9%)	0.82
Prior heart failure – no. (%)	26 (4.2%)	23 (3.7%)	0.65
Prior cerebrovascular disease – no. (%)	79 (12.9%)	72 (11.7%)	0.52
Prior peripheral vascular disease (PVD) – no. (%)	38 (6.2%)	31 (5.0%)	0.38
Mean body mass index (kg/m ²) ‡	30.7 ± 5.9	30.9 ± 6.3	0.70
Degree of ischemia on stress test, as assessed by core laboratory – no./total no. (%)			0.73
None	36/592 (6.1%)	28/594 (4.7%)	
Mild	43/592 (7.3%)	46/594 (7.7%)	
Moderate	276/592 (46.6%)	286/594 (48.1%)	
Severe	237/592 (40.0%)	234/594 (39.4%)	
Baseline SAQ Summary Score§	78.2 ± 19.0	79.2 ± 19.5	0.21
Baseline SAQ Angina Frequency Score§	84.6 ± 19.4	85.6 ± 18.5	0.47
Baseline Rose Dyspnea Scale Score¶	1.2 ± 1.4	1.2 ± 1.4	0.80
Baseline EQ-5D Visual Analog Scale	70.0 ± 19.9	70.5 ± 20.1	0.55
*includes those who completed a baseline assessment and at least one follow-up assessment.			
† Race was reported by the participant.			
‡ Body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters.			
§ On the Seattle Angina Questionnaire (SAQ), the Summary Score is obtained by averaging the SAQ Angina Frequency, SAQ Quality of Life, and SAQ Physical Limitation scores; SAQ scores range from 0 to 100, with higher scores indicating better health status.			
¶ On the Rose Dyspnea Scale, scores range from 0 to 4, with higher scores indicating dyspnea with milder activities.			
On the European Quality of Life – 5 Dimensions (EQ-5D) visual analogue scale, scores range from 0 to 100, with higher scores indicating better health status.			

Supplement Table 2: Comparison of Baseline Characteristics of North American and International Patients in the ISCHEMIA Comprehensive QOL Substudy*

Patient Characteristics	North America QOL Population (N=1234)	International QOL Population (N=585)	P-value
Age at randomization – year	66.2 ± 8.7	66.8 ± 8.8	0.04
Male sex – no.(%)	997 (80.8%)	472 (80.7%)	0.96
White race† – no./total no. (%)	1,011/1,218 (83.0%)	505/584 (86.5%)	<.001
Hypertension – no.(%)	994 (80.6%)	433 (74.1%)	0.002
Diabetes – no.(%)	522 (42.3%)	226 (38.6%)	0.14
Previous myocardial infarction – no.(%)	241 (19.6%)	113 (19.3%)	0.87
New onset of angina over the past 3 months – no./total (%)	194/1,098 (17.7%)	121/565 (21.4%)	0.07
Prior heart failure – no. (%)	49 (4.0%)	18 (3.1%)	0.34
Prior cerebrovascular disease – no. (%)	151 (12.3%)	40 (6.8%)	<.001
Prior peripheral vascular disease – no. (%)	69 (5.6%)	27 (4.6%)	0.38
Mean body mass index (kg/m ²) ‡	30.8 ± 6.1	28.2 ± 4.2	<.01
Degree of ischemia on stress test, as assessed by core laboratory – no./total no. (%)			<.001
None	64/1,186 (5.4%)	21/524 (4.0%)	
Mild	89/1,186 (7.5%)	29/524 (5.5%)	
Moderate	562/1,186 (47.4%)	191/524 (36.5%)	
Severe	471/1,186 (39.7%)	283/524 (54.0%)	
Baseline SAQ Summary Score§	78.7 ± 19.2	78.5 ± 16.9	0.15
Baseline SAQ Angina Frequency Score§	85.1 ± 18.9	85.7 ± 16.6	0.71
Baseline Rose Dyspnea Scale Score¶	1.2 ± 1.4	0.9 ± 1.1	<.01
Baseline EQ-5D Visual Analog Scale	70.3 ± 20.0	71.4 ± 39.3	0.26

*includes those who completed a baseline assessment and at least one follow-up assessment.

† Race was reported by the participant.

‡ Body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters.

§ On the Seattle Angina Questionnaire (SAQ), the Summary Score is obtained by averaging the SAQ Angina Frequency, SAQ Quality of Life, and SAQ Physical Limitation scores.

¶ On the Rose Dyspnea Scale, scores range from 0 to 4, with higher scores indicating dyspnea with milder activities.

|| On the EQ-5D visual analogue scale, scores range from 0 to 100, with higher scores indicating better health status.

Supplement Table 3: Baseline Characteristics in the ISCHEMIA Comprehensive QOL Substudy and the Portion of ISCHEMIA Patients Not Participating in the Comprehensive QOL Substudy

Descriptor	Overall (N = 5179)	Patients in QoL substudy (N = 1819)	Remaining patients (not in QoL substudy) (N = 3360)	p-value
Demographics				
Age at Randomization (yrs)				<.001
N	5179	1819	3360	
Median (Q1, Q3)	64 (58, 70)	67 (61, 72)	63 (56, 69)	
Sex				<.001
Male	4,011 / 5,179 (77.4%)	1,469 / 1,819 (80.8%)	2,542 / 3,360 (75.7%)	
Female	1,168 / 5,179 (22.6%)	350 / 1,819 (19.2%)	818 / 3,360 (24.3%)	
Race				<.001
American Indian or Alaskan Native	13 / 5,129 (0.3%)	4 / 1,802 (0.2%)	9 / 3,327 (0.3%)	
Asian	1,485 / 5,129 (29.0%)	135 / 1,802 (7.5%)	1,350 / 3,327 (40.6%)	
Native Hawaiian or Other Pacific Islander	12 / 5,129 (0.2%)	9 / 1,802 (0.5%)	3 / 3,327 (0.1%)	
Black or African American	204 / 5,129 (4.0%)	132 / 1,802 (7.3%)	72 / 3,327 (2.2%)	
White	3,403 / 5,129 (66.3%)	1,516 / 1,802 (84.1%)	1,887 / 3,327 (56.7%)	
Multiple Races Reported	12 / 5,129 (0.2%)	6 / 1,802 (0.3%)	6 / 3,327 (0.2%)	
Ethnicity				0.002
Hispanic or Latino	763 / 4,815 (15.8%)	310 / 1,717 (18.1%)	453 / 3,098 (14.6%)	
Not Hispanic or Latino	4,052 / 4,815 (84.2%)	1,407 / 1,717 (81.9%)	2,645 / 3,098 (85.4%)	
Clinical History				
Hypertension	3,789 / 5,161 (73.4%)	1,427 / 1,817 (78.5%)	2,362 / 3,344 (70.6%)	<.001
Diabetes	2,164 / 5,179 (41.8%)	748 / 1,819 (41.1%)	1,416 / 3,360 (42.1%)	0.477
Prior MI	991 / 5,162 (19.2%)	354 / 1,812 (19.5%)	637 / 3,350 (19.0%)	0.650
Prior PCI	1,050 / 5,175 (20.3%)	463 / 1,816 (25.5%)	587 / 3,359 (17.5%)	<.001
Prior CABG	203 / 5,179 (3.9%)	98 / 1,819 (5.4%)	105 / 3,360 (3.1%)	<.001
Atrial fibrillation/atrial flutter	221 / 5,173 (4.3%)	100 / 1,818 (5.5%)	121 / 3,355 (3.6%)	0.001
Non-Cardiac Vascular and Comorbidity History				
Prior transient ischemia attack	114 / 5,165 (2.2%)	68 / 1,814 (3.7%)	46 / 3,351 (1.4%)	<.001
Prior Stroke	151 / 5,178 (2.9%)	74 / 1,819 (4.1%)	77 / 3,359 (2.3%)	<.001
Prior cerebrovascular disease or peripheral artery disease	542 / 5,159 (10.5%)	265 / 1,810 (14.6%)	277 / 3,349 (8.3%)	<.001
Prior TIA, prior stroke, or prior PAD	542 / 5,179 (10.5%)	265 / 1,819 (14.6%)	277 / 3,360 (8.2%)	<.001
Qualifying Stress Test Core Lab Interpretation				
Ischemia Severity by Imaging Modality				

Descriptor	Overall (N = 5179)	Patients in QoL substudy (N = 1819)	Remaining patients (not in QoL substudy) (N = 3360)	p-value
Stress Imaging Overall (severity)				<.001
Severe	2,797 / 5,105 (54.8%)	826 / 1,812 (45.6%)	1,971 / 3,293 (59.9%)	
Moderate	1,702 / 5,105 (33.3%)	772 / 1,812 (42.6%)	930 / 3,293 (28.2%)	
Mild	352 / 5,105 (6.9%)	124 / 1,812 (6.8%)	228 / 3,293 (6.9%)	
None	254 / 5,105 (5.0%)	90 / 1,812 (5.0%)	164 / 3,293 (5.0%)	
Exercise Tolerance Test (ETT)				<.001
Severe	1,051 / 1,214 (86.6%)	72 / 102 (70.6%)	979 / 1,112 (88.0%)	
Moderate	101 / 1,214 (8.3%)	19 / 102 (18.6%)	82 / 1,112 (7.4%)	
Mild	34 / 1,214 (2.8%)	6 / 102 (5.9%)	28 / 1,112 (2.5%)	
None	28 / 1,214 (2.3%)	5 / 102 (4.9%)	23 / 1,112 (2.1%)	
CCTA Findings				
Any Obstructive Disease >=50% Stenosis by CCTA	3,832 / 3,905 (98.1%)	1,489 / 1,521 (97.9%)	2,343 / 2,384 (98.3%)	0.388
Multi-vessel disease >=50% stenosis by CCTA	2,679 / 3,909 (68.5%)	1,040 / 1,521 (68.4%)	1,639 / 2,388 (68.6%)	0.978
Vessels >=50% stenosis by CCTA				0.229
1	697 / 3,905 (17.8%)	270 / 1,521 (17.8%)	427 / 2,384 (17.9%)	
2	938 / 3,905 (24.0%)	380 / 1,521 (25.0%)	558 / 2,384 (23.4%)	
3+	1,347 / 3,905 (34.5%)	497 / 1,521 (32.7%)	850 / 2,384 (35.7%)	
Angina and Heart Failure History				
Participant has ever had angina	4,641 / 5,179 (89.6%)	1,500 / 1,819 (82.5%)	3,141 / 3,360 (93.5%)	<.001
Angina over the past month				<.001
None	1,035 / 5,177 (20.0%)	557 / 1,818 (30.6%)	478 / 3,359 (14.2%)	
I	1,389 / 5,177 (26.8%)	563 / 1,818 (31.0%)	826 / 3,359 (24.6%)	
II	2,522 / 5,177 (48.7%)	634 / 1,818 (34.9%)	1,888 / 3,359 (56.2%)	
III	230 / 5,177 (4.4%)	63 / 1,818 (3.5%)	167 / 3,359 (5.0%)	
IV	1 / 5,177 (0.0%)	1 / 1,818 (0.1%)	0 / 3,359 (0.0%)	
New Onset of Angina Over the Past 3 Months	855 / 4,918 (17.4%)	315 / 1,663 (18.9%)	540 / 3,255 (16.6%)	0.040
Angina began or became more frequent over the past 3 months	1,355 / 5,167 (26.2%)	566 / 1,807 (31.3%)	789 / 3,360 (23.5%)	<.001
Prior Heart Failure	206 / 5,179 (4.0%)	67 / 1,819 (3.7%)	139 / 3,360 (4.1%)	0.425
Continuous ejection fraction (%)				<.001
N	4637	1687	2950	

Descriptor	Overall (N = 5179)	Patients in QoL substudy (N = 1819)	Remaining patients (not in QoL substudy) (N = 3360)	p-value
Median (Q1, Q3)	60 (55, 65)	60 (55, 65)	60 (55, 65)	
Ejection fraction at peak stress				0.087
N	3077	1527	1550	
Median (Q1, Q3)	58 (51, 65)	57 (51, 65)	58 (51, 65)	
NYHA CLASS				0.056
None	3,163 / 5,179 (61.1%)	1,092 / 1,819 (60.0%)	2,071 / 3,360 (61.6%)	
NYHA Class I	999 / 5,179 (19.3%)	441 / 1,819 (24.2%)	558 / 3,360 (16.6%)	
NYHA Class II	1,017 / 5,179 (19.6%)	286 / 1,819 (15.7%)	731 / 3,360 (21.8%)	
Baseline angina frequency				0.865
Daily (score 0-30)	38 / 1,869 (2.0%)	37 / 1,815 (2.0%)	1 / 54 (1.9%)	
Weekly (score 31-60)	253 / 1,869 (13.5%)	250 / 1,815 (13.8%)	3 / 54 (5.6%)	
Monthly (score 61-99)	728 / 1,869 (39.0%)	699 / 1,815 (38.5%)	29 / 54 (53.7%)	
None (score = 100)	850 / 1,869 (45.5%)	829 / 1,815 (45.7%)	21 / 54 (38.9%)	

CCS=Canadian Cardiovascular Society, CABG=coronary artery bypass grafting surgery, CCTA=coronary computed tomography angiography, NYHA=New York Heart Association, N=number, PAD=peripheral artery disease, PCI=percutaneous coronary intervention, Q1=quartile 1, Q2=quartile 2, TIA=transient ischemic attack

Supplement Table 4: Moderate to Severe Depression in the ISCHEMIA Comprehensive QOL Substudy

PHQ-8	Invasive Strategy (N=907)	Conservative Strategy (N=912)	P-value
PHQ-8 Score ≥ 10 = Moderate to Severe Depression			
Baseline			
Number of patients with a complete PHQ-8 score	847	842	
Patients with moderate to severe depression	97 (11.5)	108 (12.8)	0.39
3 month			
Number of patients with a complete PHQ-8 score	777	778	
Patients with moderate to severe depression	72 (9.3%)	59 (7.6%)	0.23
12 month			
Number of patients with a complete PHQ-8 score	764	756	
Patients with moderate to severe depression	69 (9.0%)	59 (7.8%)	0.39
24 month			
Number of patients with a complete PHQ-8 score	565	558	
Patients with moderate to severe depression	43 (7.6%)	57 (10.2%)	0.13
36 month			
Number of patients with a complete PHQ-8 score	386	385	
Patients with moderate to severe depression	38 (9.8%)	37 (9.6%)	0.91
Close-out			
Number of patients with a complete PHQ-8 score	555	452	
Patients with moderate to severe depression	45 (8.1%)	42 (7.3%)	0.63

Supplement Table 5: Seattle Angina Questionnaire Outcomes in the ISCHEMIA Comprehensive QOL Substudy Stratified by Baseline Angina Frequency Score

A) With Baseline Angina Frequency Score of 0 to 80

	Invasive Strategy			Conservative Strategy			Adjusted Difference (95% CI)
	Median [q1 q3]	Mean (SD)	N 372	Median [q1 q3]	Mean (SD)	N 372	
SAQ Summary Score							
Scale: 0 to100; higher scores indicating greater health status							
Baseline	65 [54, 73]	62.6 (14.4)	372	63 [53, 74]	62.0 (15.4)	372	0.7 (-1.5, 2.8)
3 month	89 [70, 96]	81.7 (18.6)	355	79 [65, 89]	75.2 (18.4)	353	6.5 (3.7, 9.2)
12 month	90 [77, 97]	84.3 (17.3)	348	84 [70, 93]	79.7 (16.9)	336	4.7 (2.2, 7.2)
24 month	91 [79, 97]	85.4 (15.7)	255	86 [74, 94]	81.9 (16.8)	247	3.4 (0.8, 6.1)
36 month	92 [81, 97]	85.1 (17.8)	172	87 [76, 94]	82.7 (16.4)	169	1.7 (-1.4, 4.8)
Close-out	92 [80, 97]	85.8 (16.8)	250	87 [76, 95]	83.1 (16.1)	257	2.2 (-0.5, 4.9)
All follow-up	91 [78, 97]	84.2 (17.4)	1380	84 [71, 94]	79.9 (17.3)	1362	3.7 (1.6, 5.8)
SAQ Physical Limitation Score							
Scale: 0 to100; higher scores indicating greater health status							
Baseline	72 [53, 86]	68.8 (21.4)	345	69 [53, 86]	68.4 (22.0)	349	0.4 (-2.9, 3.6)
3 month	92 [67, 100]	81.3 (23.2)	307	85 [64, 97]	78.6 (22.3)	303	3.3 (-0.2, 6.8)
12 month	94 [75, 100]	84.8 (21.1)	310	89 [69, 100]	81.0 (22.2)	298	4.1 (0.8, 7.5)
24 month	96 [72, 100]	84.3 (21.2)	229	92 [69, 100]	81.5 (21.9)	218	2.9 (-0.8, 6.6)
36 month	94 [79, 100]	83.3 (24.1)	153	86 [72, 100]	79.7 (24.0)	150	2.4 (-2.1, 6.9)
Close-out	97 [81, 100]	85.4 (22.3)	219	92 [72, 100]	82.1 (22.4)	222	3.2 (-0.6, 7.0)
All follow-up	94 [75, 100]	83.7 (22.3)	1218	89 [69, 100]	80.5 (22.5)	1191	3.2 (0.2, 6.1)
SAQ Angina Frequency Score							
Scale: 0 to100; higher scores indicating greater health status							
Baseline	70 [60, 80]	65.9 (15.5)	372	70 [60, 80]	66.3 (15.1)	372	-0.4 (-2.6, 1.8)
3 month	100 [80, 100]	87.3 (18.8)	354	90 [70, 100]	81.4 (20.6)	353	6.1 (3.2, 9.0)
12 month	100 [80, 100]	89.1 (17.4)	346	90 [80, 100]	85.4 (18.1)	336	3.8 (1.1, 6.4)
24 month	100 [90, 100]	90.9 (16.4)	255	100 [80, 100]	88.3 (16.9)	246	2.4 (-0.4, 5.2)
36 month	100 [90, 100]	91.9 (16.5)	171	100 [80, 100]	89.3 (16.6)	169	1.7 (-1.5, 5.0)
Close-out	100 [80, 100]	90.7 (15.9)	250	100 [80, 100]	88.4 (17.8)	256	1.8 (-1.1, 4.7)
All follow-up	100 [80, 100]	89.6 (17.3)	1376	90 [80, 100]	85.9 (18.6)	1360	3.2 (1.2, 5.1)
SAQ Quality of Life Score							
Scale: 0 to100; higher scores indicating greater health status							
Baseline	50 [42, 67]	53.5 (19.8)	372	50 [38, 67]	51.9 (22.2)	370	1.6 (-1.4, 4.6)
3 month	83 [67, 92]	76.1 (22.6)	352	67 [50, 83]	66.4 (22.8)	351	9.6 (6.3, 12.9)
12 month	83 [67, 96]	78.8 (21.2)	340	75 [58, 92]	72.6 (21.8)	332	6.3 (3.1, 9.5)
24 month	83 [67, 92]	81.0 (18.8)	254	83 [67, 92]	75.5 (21.7)	244	5.7 (2.3, 9.1)
36 month	83 [67, 100]	80.1 (21.6)	171	83 [67, 92]	77.7 (20.9)	161	3.2 (-0.9, 7.3)
Close-out	92 [67, 100]	81.3 (19.9)	243	83 [67, 92]	78.8 (19.0)	244	1.8 (-1.5, 5.1)
All follow-up	83 [67, 92]	79.1 (21.0)	1360	75 [58, 92]	73.2 (21.9)	1332	5.3 (2.8, 7.8)
SAQ Treatment Satisfaction							
Scale: 0 to100; higher scores indicating greater health status							

Baseline	81 [75, 100]	82.8 (15.8)	364	81 [69, 100]	81.8 (17.7)	360	0.9 (-1.5, 3.3)
3 month	100 [81, 100]	90.3 (13.1)	333	88 [81, 100]	86.8 (15.4)	329	3.2 (-1.1, 5.4)
12 month	100 [81, 100]	91.4 (12.8)	332	94 [81, 100]	87.3 (16.1)	325	4.1 (-1.9, 6.3)
24 month	100 [84, 100]	91.9 (12.2)	248	97 [81, 100]	89.1 (14.8)	236	3.1 (0.8, 5.4)
36 month	100 [88, 100]	91.6 (14.2)	170	100 [81, 100]	91.1 (13.0)	162	0.1 (-2.7, 2.8)
Close-out	100 [88, 100]	91.1 (16.3)	241	100 [81, 100]	90.8 (13.7)	244	-0.2 (-2.8, 2.3)
All follow-up	100 [81, 100]	91.2 (13.6)	1324	94 [81, 100]	88.6 (15.0)	1296	2.0 (0.4, 3.7)

B) With Baseline Angina Frequency Score of 81 to 100

	Invasive Strategy			Conservative Strategy			Adjusted Difference (95% CI)
	Median [q1 q3]	Mean (SD)	N 533	Median [q1 q3]	Mean (SD)	N 538	
SAQ Summary Score							
Scale: 0 to100; higher scores indicating greater health status							
Baseline	87 [79, 94]	85.3 (11.4)	533	89 [81, 94]	87.1 (9.9)	538	-1.9 (-3.2, -0.6)
3 month	92 [83, 97]	87.7 (13.6)	506	92 [84, 97]	88.8 (11.3)	505	-1.2 (-2.7, 0.3)
12 month	94 [86, 99]	90.6 (11.0)	483	94 [85, 97]	90.0 (11.5)	487	0.7 (-0.7, 2.1)
24 month	94 [88, 100]	91.0 (11.4)	359	94 [86, 97]	90.5 (11.1)	353	0.5 (-1.1, 2.0)
36 month	94 [83, 100]	89.9 (12.0)	239	95 [89, 98]	90.9 (12.0)	241	-0.7 (-2.7, 1.2)
Close-out	94 [86, 99]	90.4 (11.3)	353	94 [87, 97]	90.7 (11.2)	360	-0.3 (-1.9, 1.3)
All follow-up	94[85, 98]	89.8 (12.0)	1940	94 [86, 97]	90.0 (11.4)	1946	-0.2 (-1.4, 0.9)
SAQ Physical Limitation Score							
Scale: 0 to100; higher scores indicating greater health status							
Baseline	89 [75, 100]	83.3 (19.2)	481	89 [78, 100]	85.0 (17.1)	486	-1.7 (-4.0, 0.6)
3 month	100 [83, 100]	87.7 (19.3)	439	97 [82, 100]	88.7 (16.5)	446	-1.0 (-3.3, 1.3)
12 month	100 [83, 100]	89.7 (17.1)	426	100 [86, 100]	90.1 (16.2)	432	-0.4 (-2.6, 1.8)
24 month	100 [88, 100]	90.4 (16.6)	308	100 [85, 100]	89.5 (17.3)	316	0.4 (-2.1, 2.9)
36 month	100 [79, 100]	86.2 (20.7)	210	97 [83, 100]	88.4 (18.8)	213	-1.3 (-4.7, 2.0)
Close-out	100 [83, 100]	89.9 (16.8)	312	100 [86, 100]	90.6 (15.4)	320	-0.6 (-3.0, 1.9)
All follow-up	100 [83, 100]	88.9 (18.1)	1695	100 [83, 100]	89.5 (16.7)	1727	-0.6 (-2.5, 1.3)
SAQ Angina Frequency Score							
Scale: 0 to100; higher scores indicating greater health status							
Baseline	100 [100, 100]	97.6 (4.3)	533	100 [100, 100]	97.9 (4.1)	538	-0.2 (-0.7, 0.3)
3 month	100 [100, 100]	95.1 (12.2)	505	100 [100, 100]	95.7 (10.3)	505	-0.5 (-1.9, 0.9)
12 month	100 [100, 100]	97.1 (9.0)	482	100 [100, 100]	96.5 (10.1)	485	0.6 (-0.6, 1.8)
24 month	100 [100, 100]	96.8 (10.7)	357	100 [100, 100]	96.1 (10.3)	352	0.6 (-0.9, 2.1)
36 month	100 [100, 100]	96.3 (10.9)	238	100 [100, 100]	96.7 (9.0)	240	-0.5 (-2.2, 1.2)
Close-out	100 [100, 100]	96.8 (9.3)	353	100 [100, 100]	96.7 (9.1)	359	0.0 (-1.3, 1.3)
All follow-up	100 [100, 100]	96.4 (10.6)	1935	100 [100, 100]	96.3 (9.9)	1941	0.0 (-0.8, 0.9)
SAQ Quality of Life Score							
Scale: 0 to100; higher scores indicating greater health status							
Baseline	75 [58, 92]	74.1 (19.3)	524	83 [67, 92]	77.7 (18.5)	522	-3.6 (-5.8, -1.3)
3 month	83 [67, 92]	80.2 (18.8)	498	83 [75, 92]	81.7 (16.9)	496	-1.6 (-3.8, 0.6)
12 month	92 [75, 100]	84.9 (16.7)	476	92 [75, 100]	83.1 (18.1)	479	1.9 (-0.3, 4.1)
24 month	92 [75, 100]	85.5 (16.3)	349	92 [75, 100]	86.0 (14.7)	342	-0.6 (-2.8, 1.6)

	36 month	92 [83, 100]	86.0 (17.0)	231	92 [83, 100]	86.7 (16.1)	233	-0.1 (-2.9, 2.6)
	Close-out	92 [75, 100]	84.7 (16.6)	340	92 [75, 100]	84.6 (17.1)	348	-0.4 (-2.8, 2.0)
	All follow-up	92 [75, 100]	83.9 (17.4)	1894	92 [75, 100]	84.0 (16.9)	1898	-0.2 (-1.8, 1.5)

SAQ Treatment Satisfaction

Scale: 0 to 100; higher scores indicating greater health status

	Baseline	94 [81, 100]	89.4 (13.2)	504	100 [81, 100]	92.4 (10.6)	498	-2.8 (-4.3, -1.3)
	3 month	100 [81, 100]	91.5 (13.2)	471	100 [88, 100]	92.1 (11.4)	479	-0.6 (-2.2, 0.9)
	12 month	100 [88, 100]	92.7 (12.5)	450	100 [81, 100]	92.2 (11.6)	465	0.4 (-1.2, 1.9)
	24 month	100 [94, 100]	93.8 (11.0)	336	100 [88, 100]	92.8 (11.2)	337	0.9 (-0.7, 2.5)
	36 month	100 [88, 100]	92.6 (12.4)	230	100 [88, 100]	92.5 (13.6)	231	0.7 (-1.6, 3.0)
	Close-out	100 [88, 100]	93.1 (12.3)	336	100 [88, 100]	92.8 (11.9)	347	0.3 (-1.4, 2.1)
	All follow-up	100 [88, 100]	92.7 (12.4)	1823	100 [88, 100]	92.4 (11.8)	1859	0.3 (-0.8, 1.4)

Supplement Table 6: Secondary Quality of Life Instruments in the ISCHEMIA Comprehensive QOL Substudy Stratified by Baseline Angina Frequency Score

A) With Baseline Angina Frequency Score of 0 to 80

	Invasive Strategy			Conservative Strategy			Adjusted Difference (95% CI)
	Median [q1, q3]	Mean (SD)	N 372	Median [q1, q3]	Mean (SD)	N 372	
Duke Activity Score Index							
Scale: 0 to 58.2; higher scores denote greater functional capacity							
Baseline	18 [7, 32]	20.3 (15.1)	228	13 [7, 26]	18.1 (14.3)	235	2.1 (-0.5, 4.8)
3 month	22 [11, 36]	24.2 (16.5)	224	21 [11, 31]	22.0 (14.2)	219	2.0 (-0.8, 4.8)
12 month	25 [13, 38]	26.3 (16.7)	230	21 [9, 37]	23.2 (16.3)	219	3.4 (0.4, 6.3)
24 month	27 [14, 39]	27.3 (16.7)	166	24 [12, 37]	25.0 (16.2)	170	2.9 (-0.2, 6.1)
36 month	26 [13, 37]	25.8 (16.9)	114	21 [11, 34]	23.2 (15.9)	113	2.9 (-0.4, 6.3)
Close-out	25 [13, 43]	26.7 (17.2)	178	21 [10, 32]	22.6 (15.2)	180	4.7 (1.7, 7.7)
All follow-up	25 [13, 38]	26.0 (16.8)	912	21 [10, 33]	23.2 (15.5)	901	3.2 (0.6, 5.7)
RAND General Health Rating							
Scale: 0 to 100; higher score indicating greater overall health							
Baseline	50 [25, 50]	44.8 (22.1)	243	50 [25, 50]	44.8 (21.6)	248	0.0 (-3.9, 3.8)
3 month	50 [25, 75]	52.1 (22.5)	227	50 [25, 50]	47.4 (23.4)	232	4.5 (0.3, 8.6)
12 month	50 [50, 75]	55.3 (23.9)	234	50 [25, 75]	49.5 (21.3)	233	6.3 (2.2, 10.4)
24 month	50 [50, 75]	56.1 (25.3)	173	50 [25, 75]	51.1 (23.1)	178	6.1 (1.3, 10.8)
36 month	50 [50, 75]	55.2 (26.1)	120	50 [25, 75]	53.0 (23.4)	123	3.3 (-2.2, 8.8)
Close-out	50 [50, 75]	56.1 (24.5)	190	50 [25, 75]	51.3 (22.0)	196	5.6 (1.1, 10.1)
All follow-up	50 [50, 75]	54.8 (24.2)	944	50 [25, 75]	50.1 (22.6)	962	5.2 (1.6, 8.7)
Rose Dyspnea Scale							
Scores range from 0 to 4, where 0 indicates no dyspnea with activity and 4 indicates significant limitations due to dyspnea							
Baseline	1 [0, 3]	1.6 (1.4)	362	1 [1, 3]	1.7 (1.4)	364	-0.1 (-0.3, 0.1)
3 month	0 [0, 2]	1.1 (1.4)	338	1 [0, 2]	1.3 (1.4)	341	-0.2 (-0.4, 0)
12 month	0 [0, 1]	0.9 (1.4)	336	1 [0, 2]	1.2 (1.4)	320	-0.3 (-0.5, -0.1)
24 month	0 [0, 1]	1.0 (1.4)	249	0 [0, 1]	1.0 (1.3)	237	0 (-0.2, 0.3)
36 month	0 [0, 1]	1.0 (1.4)	166	1 [0, 2]	1.2 (1.4)	159	-0.1 (-0.4, 0.2)
Close-out	0 [0, 2]	0.9 (1.4)	238	1 [0, 2]	1.2 (1.5)	234	-0.3 (-0.5, 0)
All follow-up	0 [0, 1]	1.0 (1.4)	1327	1 [0, 2]	1.2 (1.4)	1291	-0.2 (-0.3, 0)
Perceived Stress Scale - 4							
Scale: 0 to 16; higher values denoting greater perceptions of stress							
Baseline	5 [2, 7]	4.5 (3.0)	243	5 [2, 8]	5.1 (3.3)	246	-0.6 (-1.2, -0.1)
3 month	3 [1, 6]	3.8 (3.1)	223	3 [1, 6]	3.8 (3.3)	224	-0.1 (-0.7, 0.5)
12 month	3 [1, 6]	3.7 (3.2)	226	3 [1, 6]	3.6 (3.1)	217	0.0 (-0.6, 0.6)
24 month	2 [1, 6]	3.5 (3.3)	162	3 [1, 6]	3.6 (3.3)	169	-0.3 (-1.0, 0.4)
36 month	4 [1, 7]	4.2 (3.6)	116	2 [0, 6]	3.3 (3.2)	110	0.6 (-0.2, 1.4)
Close-out	2 [0, 6]	3.2 (3.3)	182	2 [0, 5]	2.8 (2.8)	173	0.2 (-0.4, 0.8)
All follow-up	3 [1, 6]	3.7 (3.3)	909	3 [1, 6]	3.5 (3.2)	893	0.1 (-0.4, 0.6)

Life Orientation Test- Revised Score								
Scale: 0 to 24; higher score indicating greater optimism								
Baseline	17 [14, 21]	16.8 (5.1)	240	17 [14, 21]	16.9 (5.1)	235	-0.1 (-1.0, 0.8)	
3 month	19 [15, 23]	18.1 (5.5)	224	19 [15, 23]	18.0 (5.2)	227	0.1 (-0.9, 1.1)	
12 month	20 [15, 24]	18.5 (5.2)	228	20 [16, 23]	19.1 (4.7)	220	-0.6 (-1.5, 0.3)	
24 month	20 [15, 24]	18.6 (5.2)	167	19 [15, 23]	18.6 (5.0)	169	-0.1 (-1.1, 1.0)	
36 month	19 [14, 24]	18.0 (5.4)	111	20 [16, 23]	19.0 (5.0)	113	-0.8 (-2.0, 0.3)	
Close-out	20 [15, 23]	18.5 (5.1)	177	21 [16, 24]	19.7 (4.3)	172	-1.1 (-2.0, -0.1)	
All follow-up	19 [15, 23]	18.3 (5.3)	907	20 [15, 23]	18.8 (4.9)	901	-0.5 (-1.3, 0.3)	
Patient Health Questionnaire-8								
Scale: 0 to 24; higher scores indicating greater severity of depression								
Baseline	3 [1, 7]	4.5 (4.8)	345	4 [1, 8]	5.4 (5.4)	346	-0.9 (-1.6, -0.1)	
3 month	2 [0, 6]	4.2 (5.1)	320	2 [0, 6]	3.9 (4.5)	313	0.2 (-0.6, 0.9)	
12 month	2 [0, 6]	3.9 (4.7)	316	2 [0, 6]	3.9 (4.5)	303	-0.1 (-0.8, 0.6)	
24 month	2 [0, 5]	3.6 (4.5)	239	2 [0, 6]	4.0 (4.7)	228	-0.3 (-1.1, 0.4)	
36 month	2 [0, 5]	3.7 (5.1)	164	2 [0, 5]	3.6 (4.7)	154	-0.2 (-1.0, 0.7)	
Close-out	1 [0, 4]	3.2 (4.2)	226	2 [0, 5]	3.5 (4.3)	233	-0.4 (-1.1, 0.3)	
All follow-up	2 [0, 5]	3.8 (4.7)	1265	2 [0, 6]	3.8 (4.5)	1231	-0.2 (-0.8, 0.4)	
EQ-5D-VAS								
Scale: 0 to 100; higher scores denote better self-reported health state								
Baseline	70 [55, 80]	67.6 (16.7)	364	70 [50, 80]	66.1 (18.5)	366	1.5 (-1.0, 4.1)	
3 month	75 [60, 85]	73.0 (17.6)	343	75 [65, 84]	72.1 (17.4)	344	1.0 (-1.6, 3.6)	
12 month	80 [67, 87]	73.9 (18.5)	342	80 [65, 85]	73.4 (18.0)	332	0.6 (-2.1, 3.3)	
24 month	80 [70, 90]	75.8 (17.3)	243	80 [70, 90]	74.6 (18.1)	242	1.2 (-1.8, 4.1)	
36 month	80 [70, 90]	75.4 (18.0)	167	80 [63, 85]	73.7 (17.1)	164	1.6 (-1.6, 4.8)	
Close-out	80 [70, 90]	76.4 (17.7)	245	75 [65, 85]	73.7 (16.0)	251	2.2 (-0.6, 5.1)	
All follow-up	80 [68, 90]	74.6 (17.9)	1340	75 [65, 85]	73.4 (17.4)	1333	1.3 (-0.9, 3.5)	

B) With Baseline Angina Frequency Score of 81 to 100

Timepoint	Invasive Strategy			Conservative Strategy			Adjusted Difference (95% CI)
	Median [q1 q3]	Mean (SD)	N 533	Median [q1 q3]	Mean (SD)	N 538	
Duke Activity Score Index							
Scale: 0 to 58.2; higher scores denote greater functional capacity							
Baseline	27 [13, 39]	28.1 (16.7)	328	30 [17, 43]	30.0 (16.2)	333	-2.2 (-4.6, 0.3)
3 month	23 [13, 37]	26.7 (16.0)	323	30 [18, 40]	29.6 (15.4)	322	-3.6 (-5.9, -1.2)
12 month	28 [13, 43]	28.7 (16.5)	306	31 [18, 43]	30.4 (15.9)	317	-1.8 (-4.3, 0.6)
24 month	27 [16, 42]	28.3 (16.3)	241	31 [15, 40]	29.4 (16.1)	241	-1.6 (-4.2, 0.9)
36 month	27 [13, 38]	26.9 (16.7)	163	29 [16, 43]	28.7 (16.6)	176	-1.7 (-4.6, 1.2)
Close-out	27 [13, 41]	27.3 (16.3)	254	29 [16, 41]	28.7 (15.7)	263	-1.1 (-3.7, 1.4)
All follow-up	27 [13, 39]	27.6 (16.3)	1287	30 [16, 43]	29.4 (15.9)	1319	-2.0 (-4.1, 0.1)
RAND General Health Rating							
Scale: 0 to 100; higher score indicating greater overall health							
Baseline	50 [50, 75]	52.1 (21.7)	348	50 [50, 75]	56.2 (21.9)	346	-4.0 (-7.2, -0.7)

	3 month	50 [50, 75]	55.9 (22.9)	337	50 [50, 75]	57.6 (21.0)	331	-1.9 (-5.2, 1.3)
	12 month	50 [50, 75]	58.0 (24.0)	319	50 [50, 75]	58.6 (22.1)	329	-1.1 (-4.6, 2.3)
	24 month	50 [50, 75]	57.8 (23.1)	259	50 [50, 75]	58.0 (22.4)	251	-0.9 (-4.6, 2.8)
	36 month	50 [50, 75]	56.1 (23.6)	173	50 [50, 75]	57.6 (22.4)	188	-3.2 (-7.5, 1.0)
	Close-out	50 [50, 75]	57.8 (24.1)	272	50 [50, 75]	56.6 (23.3)	283	1.1 (-2.7, 4.8)
	All follow-up	50 [50, 75]	57.2 (23.5)	1360	50 [50, 75]	57.7 (22.2)	1382	-1.2 (-4.0, 1.6)

Rose Dyspnea Scale

Scores range from 0 to 4, where 0 indicates no dyspnea with activity and 4 indicates significant limitations due to dyspnea

	Baseline	0 [0, 1]	0.8 (1.2)	524	0 [0, 1]	0.8 (1.1)	528	0 (-0.1, 0.2)
	3 month	0 [0, 1]	0.7 (1.2)	480	0 [0, 1]	0.7 (1.1)	490	0 (-0.1, 0.1)
	12 month	0 [0, 1]	0.6 (1.2)	470	0 [0, 1]	0.6 (1.1)	471	0 (-0.1, 0.1)
	24 month	0 [0, 1]	0.7 (1.2)	343	0 [0, 1]	0.6 (1.1)	337	0.1 (-0.1, 0.2)
	36 month	0 [0, 1]	0.7 (1.2)	230	0 [0, 1]	0.7 (1.2)	231	0 (-0.2, 0.2)
	Close-out	0 [0, 1]	0.7 (1.2)	339	0 [0, 1]	0.8 (1.2)	344	0 (-0.2, 0.1)
	All follow-up	0 [0, 1]	0.7 (1.2)	1862	0 [0, 1]	0.7 (1.1)	1873	0 (-0.1, 0.1)

Perceived Stress Scale - 4

Scale: 0 to 16; higher values denoting greater perceptions of stress

	Baseline	4 [1, 6]	4.0 (3.0)	346	4 [1, 6]	3.9 (3.1)	346	0.0 (-0.5, 0.5)
	3 month	2 [0, 5]	3.2 (3.1)	314	2 [0, 5]	2.8 (2.9)	324	0.3 (-0.1, 0.8)
	12 month	2 [0, 5]	3.2 (3.2)	311	2 [0, 5]	3.0 (3.2)	317	0.2 (-0.3, 0.7)
	24 month	3 [1, 6]	3.4 (3.1)	241	2 [0, 6]	3.2 (3.1)	239	0.2 (-0.3, 0.8)
	36 month	3 [1, 6]	3.4 (3.0)	165	2 [0, 5]	2.8 (3.0)	180	0.6 (0.0, 1.2)
	Close-out	2 [0, 6]	3.0 (3.1)	255	1 [0, 5]	2.6 (3.1)	265	0.4 (-0.1, 0.9)
	All follow-up	2 [0, 5]	3.2 (3.1)	1286	2 [0, 5]	2.9 (3.1)	1325	0.4 (0.0, 0.7)

Life Orientation Test- Revised Score

Scale: 0 to 24; higher score indicating greater optimism

	Baseline	18 [14, 22]	17.8 (4.7)	340	18 [14, 22]	17.7 (4.9)	335	0.3 (-0.4, 1.0)
	3 month	20 [15, 23]	18.5 (5.1)	313	20 [15, 23]	18.7 (4.6)	320	-0.1 (-0.8, 0.7)
	12 month	20 [16, 23]	18.7 (5.0)	310	20 [16, 23]	19.2 (4.5)	311	-0.7 (-1.4, 0.0)
	24 month	20 [15, 23]	18.6 (4.7)	240	20 [15, 24]	18.6 (5.3)	235	-0.1 (-0.9, 0.7)
	36 month	20 [15, 24]	18.9 (4.8)	163	21 [16, 24]	19.3 (5.5)	173	-0.1 (-1.1, 0.8)
	Close-out	20 [16, 24]	19.3 (4.8)	248	21 [16, 23]	19.1 (4.9)	260	0.2 (-0.6, 0.9)
	All follow-up	20 [16, 23]	18.8 (4.9)	1274	20 [16, 24]	19.0 (4.9)	1299	-0.2 (-0.8, 0.4)

Patient Health Questionnaire-8

Scale: 0 to 24; higher scores indicating greater severity of depression

	Baseline	2 [0, 5]	3.5 (4.2)	500	2 [0, 4]	3.1 (3.8)	494	0.3 (-0.2, 0.8)
	3 month	1 [0, 4]	2.9 (4.1)	455	1 [0, 4]	2.7 (3.4)	463	0.2 (-0.3, 0.7)
	12 month	1 [0, 4]	2.7 (3.8)	446	1 [0, 4]	2.6 (3.9)	452	0.1 (-0.4, 0.6)
	24 month	1 [0, 4]	2.8 (3.7)	325	1 [0, 4]	2.9 (3.9)	329	0.0 (-0.5, 0.5)
	36 month	1 [0, 5]	2.9 (4.0)	222	1 [0, 3]	2.8 (4.2)	230	0.2 (-0.4, 0.8)
	Close-out	1 [0, 4]	2.7 (3.9)	327	1 [0, 3]	2.5 (3.8)	337	0.3 (-0.3, 0.8)
	All follow-up	1 [0, 4]	2.8 (3.9)	1775	1 [0, 4]	2.7 (3.8)	1811	0.2 (-0.2, 0.6)

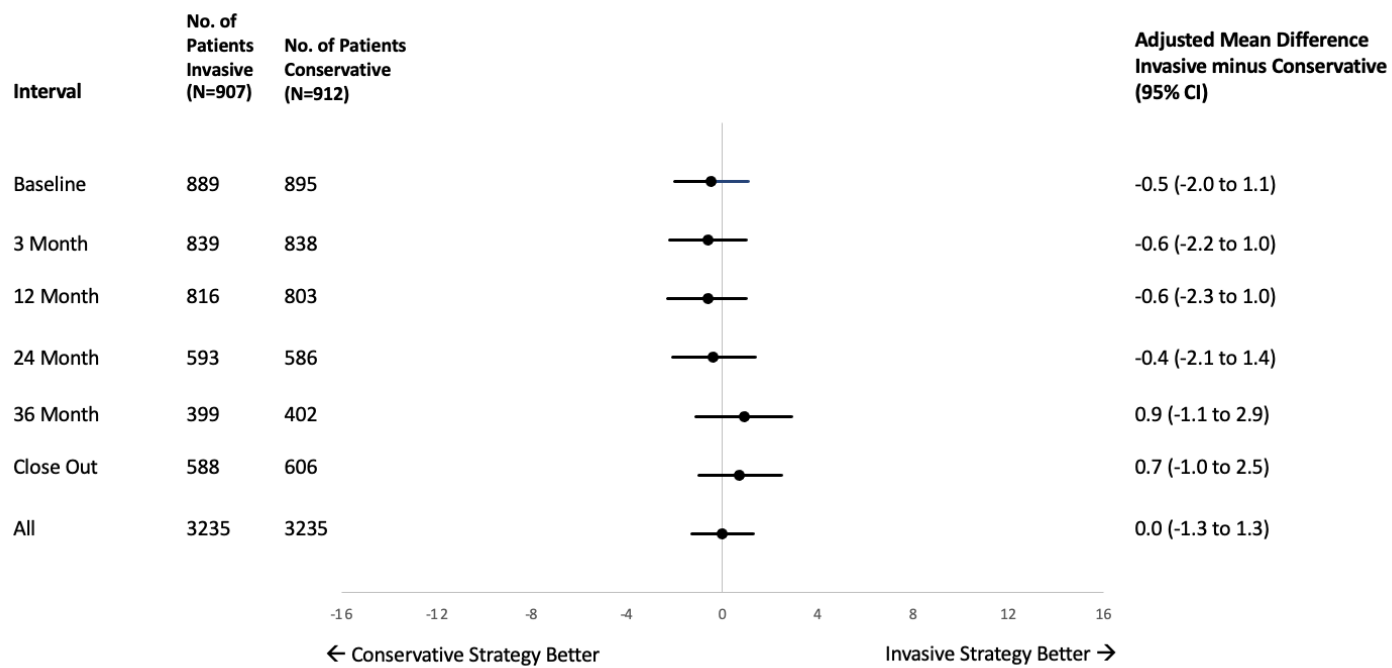
EQ-5D-VAS

Scale: 0 to 100; higher scores denote better self-reported health state

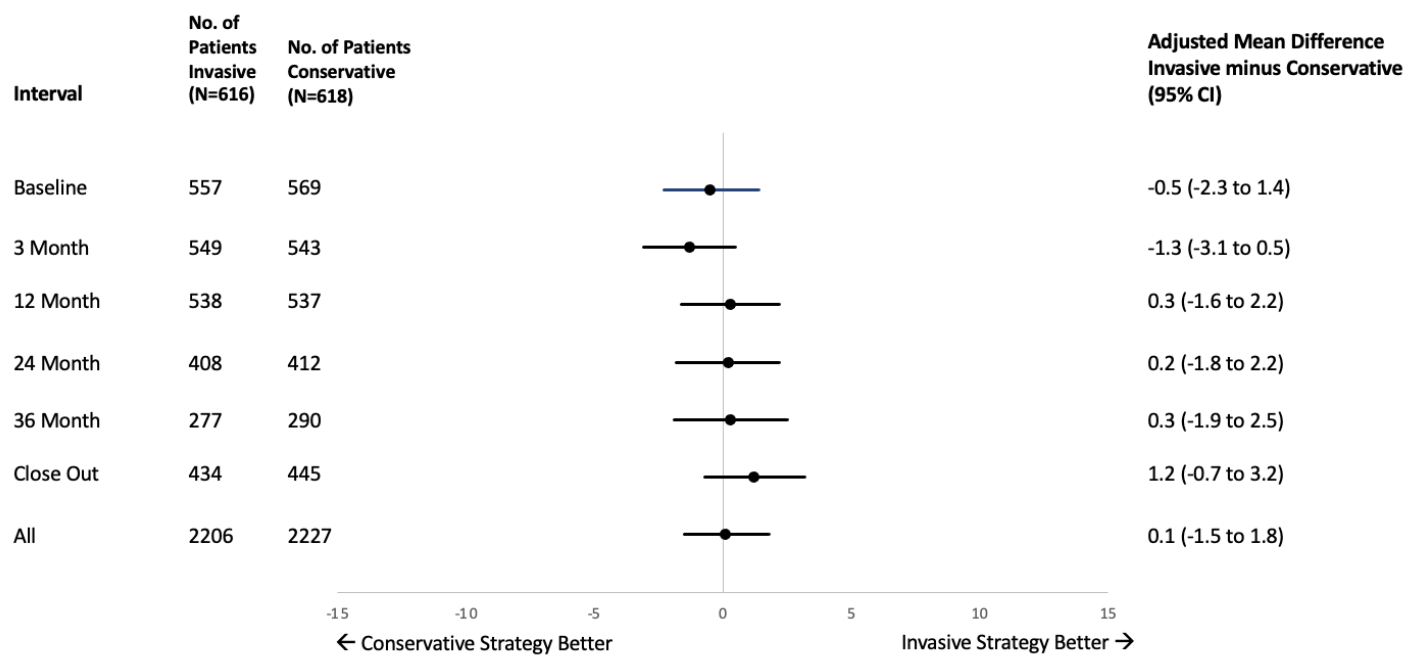
	Baseline	75 [65, 85]	74.0 (16.0)	523	80 [70, 85]	75.8 (15.0)	527	-1.8 (-3.6, 0.1)
	3 month	80 [70, 90]	76.0 (16.6)	494	80 [70, 90]	77.4 (14.4)	492	-1.7 (-3.6, 0.2)
	12 month	80 [70, 90]	76.9 (16.2)	472	80 [75, 90]	78.3 (15.6)	469	-1.4 (-3.4, 0.6)

24 month	80 [70, 90]	77.2 (16.7)	349	80 [74, 90]	79.0 (14.4)	343	-1.4 (-3.5, 0.7)
36 month	80 [70, 90]	78.4 (15.8)	232	80 [70, 90]	77.9 (16.4)	237	0.5 (-2.0, 3.1)
Close-out	80 [70, 90]	77.3 (16.2)	341	80 [70, 90]	77.3 (15.3)	353	-0.1 (-2.3, 2.1)
All follow-up	80 [70, 90]	77.0 (16.3)	1888	80 [70, 90]	77.9 (15.1)	1894	-0.8 (-2.4, 0.8)

Supplement Figure 1: Treatment Differences in EQ-5D Visual Analog Scale Outcomes in the ISCHEMIA Comprehensive QOL Substudy

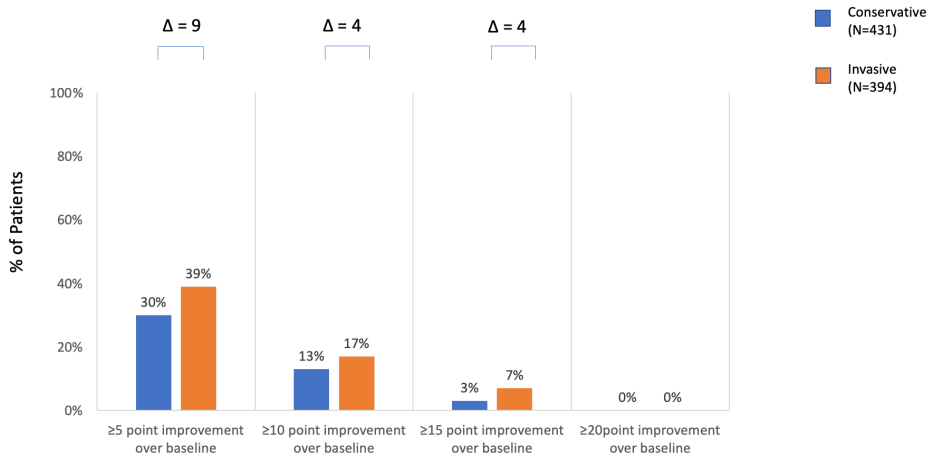


Supplement Figure 3: Treatment Differences in DASI Outcomes in the ISCHEMIA Comprehensive QOL Substudy, North America

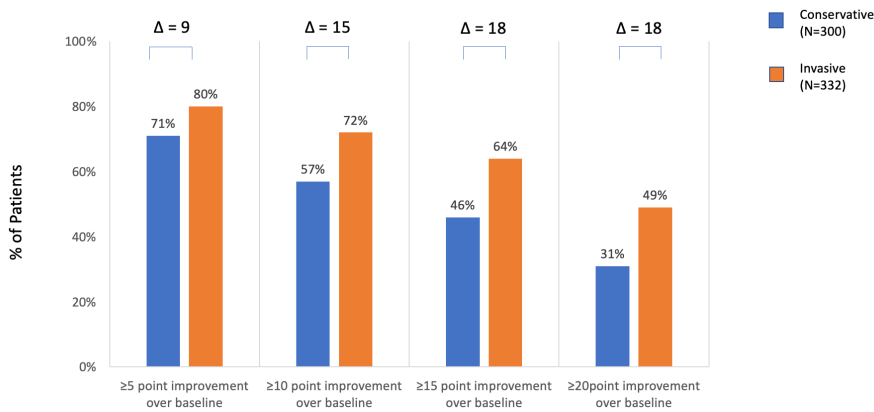


Supplement Figure 6: 12-Month Improvement in Seattle Angina Summary Scores in Patients with Mild, Moderate, and Severe QOL Impairment at Baseline

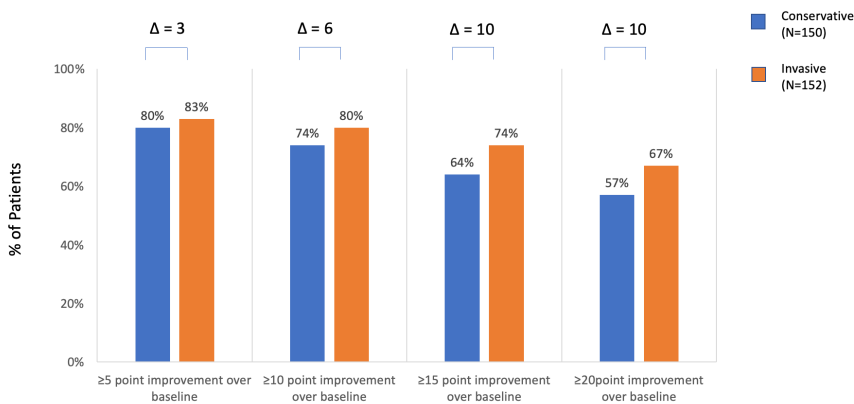
A. Mild QOL Impairment at Baseline (SAQ Summary Score 81-100)



B. Moderate QOL Impairment at Baseline (SAQ Summary Score 61-80)

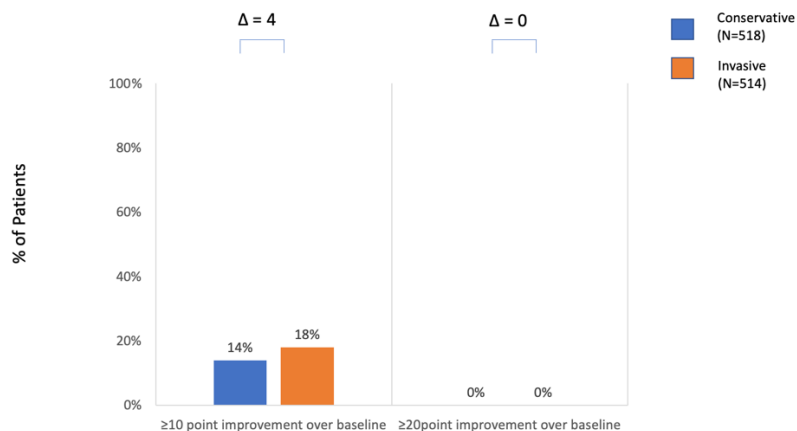


C. Severe QOL Impairment at Baseline (SAQ Summary Score ≤60)

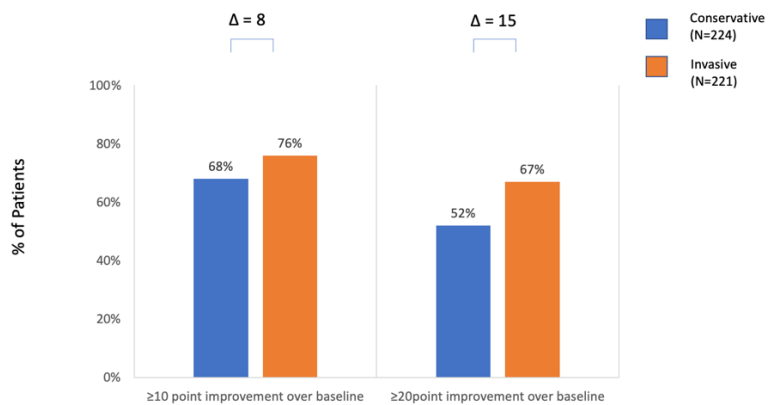


Supplement Figure 7: 12-Month Improvement in SAQ Angina Frequency Scores in Patients with Mild, Moderate, and Severe Limitations at Baseline

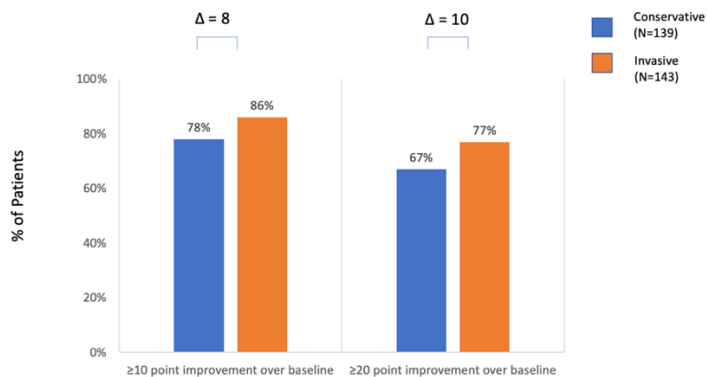
A. Mild Angina Frequency at Baseline (SAQ AF Score 81-100)



B. Moderate Angina Frequency at Baseline (SAQ AF Score 61-80)

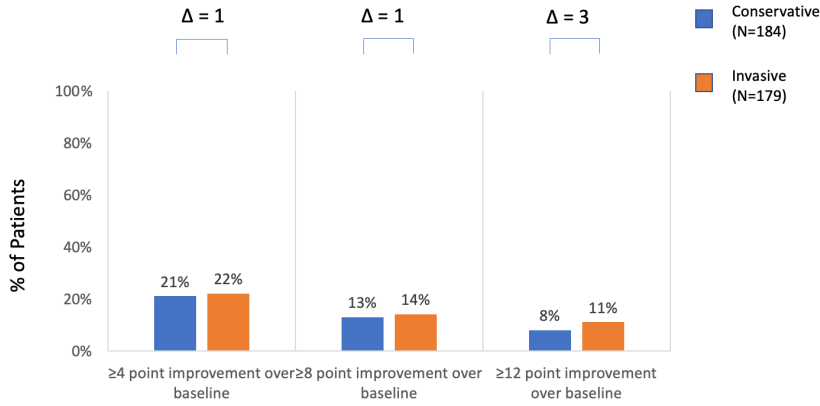


C. Severe Angina Frequency at Baseline (SAQ AF Score ≤60)

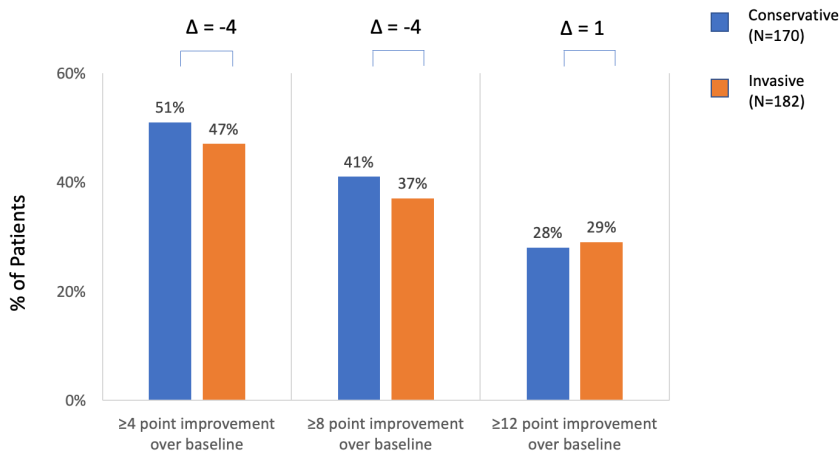


Supplement Figure 8: 12-Month Improvement in Duke Activity Status Index Scores in Patients with Mild, Moderate, and Severe Limitations at Baseline

A. Mild Physical Limitations at Baseline (DASI 31.5 to 58.2)



B. Moderate Physical Limitations at Baseline (DASI 13.5 to 31.4)



C. Severe Physical Limitations at Baseline (DASI 0 to 13.4)

