Impact Of Completeness Of Revascularization On Quality-of-life In Patients With Stable Ischemic Heart Disease:

Insights From The ISCHEMIA Trial

ISCHEMIA

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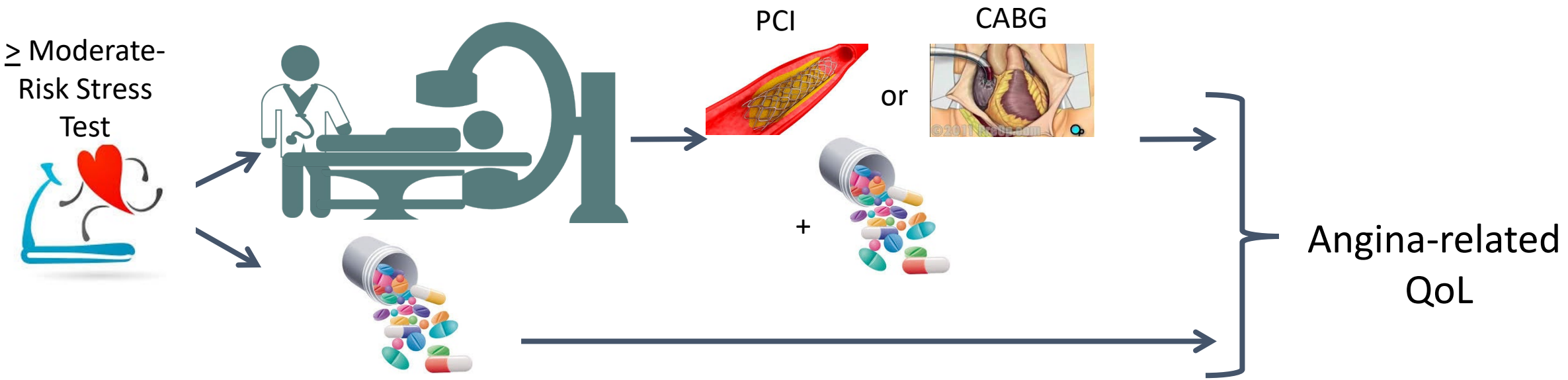
Disclosures

None

Design of the ISCHEMIA Trial

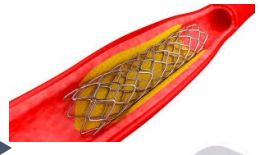


Key Clinical Question

Does the Completeness of Revascularization (Anatomic or Functional) Influence Outcomes?

≥ Moderate-Risk Stress Test

PCI



or

CABG

+

Angina-related QoL

ACC.21

ISCHEMIA

Angiographic Core Laboratory* Assessment of Anatomic and Functional Completeness of Revascularization After PCI and CABG

- **PCI:** CR assessed by review of pre- and post-procedure angiograms (includes planned staged procedures)
- **CABG:** CR assessed by review of pre-procedure angiograms and CABG procedure reports; accounts for diseased vessel segments and side branches

- **Anatomic CR:** Revasc of all lesions with QCA RVD ≥2.0 mm and QCA DS ≥50%
- **Functional CR:** Revasc of all lesions with QCA RVD ≥2.0 mm and:
  - Localizing FFR/iFR ≤0.80/0.89 plus QCA DS ≥30%
  - Localizing non-invasive ischemia in the vessel distribution plus QCA DS ≥50%
  - Non-localizing severe ischemia by ETT plus QCA DS ≥60%
  - QCA DS ≥70%

Modified from Ali Z et al. J Am Heart Assoc. 2021:e020110. doi: 10.1161/JAHA.120.020110

Key Outcome Measures

Seattle Angina Questionnaire – 7

- Angina Frequency
- Quality of Life
- Physical Limitations

} SAQ Summary Score

Rose Dyspnea Score (RDS)

Primary Outcome
Adjusted SAQ Summary Score at 1 year

Objectives

Objective 1: Compare complete (CR) vs. incomplete revascularization (ICR) *among invasively managed*, *revascularized* patients

- Proportional odds model used to adjust for 24 clinical and angiographic variables
- Results expressed as odds ratio of better QOL for CR vs. ICR

Objective 2: Compare the expected outcomes of CR vs. conservative management in the overall ISCHEMIA population

- Propensity weighting used to rebalance patient characteristics for CR to mirror the overall population
- Results expressed as expected difference in mean QOL scores.

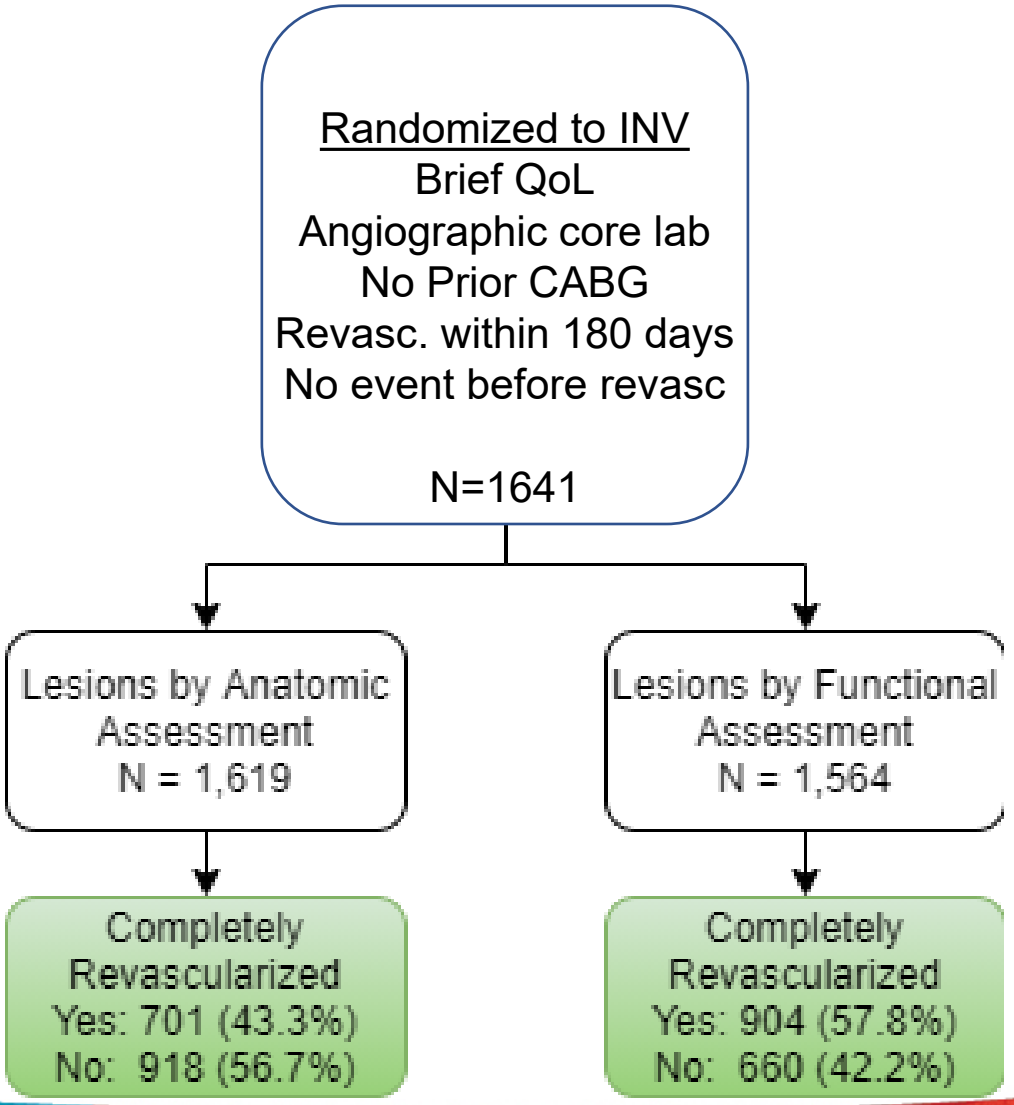
Objectives (cont)

Analyses were performed for all patients and patients stratified by:

- Baseline angina frequency
- Baseline ischemia
- Presence of CTOs

Objective 1: CR vs ICR in Invasively Managed Patients

Patient Flow



CR vs ICR in Invasively Managed Patients

Select Baseline Clinical Characteristics

	Anatomic CR		P-Value	Functional CR		P-Value
	CR n = 701	ICR n = 918		CR n = 904	ICR n = 660	
Age	63.4 ± 9.7	64.1 ± 9.2	0.147	63.6 ± 9.5	64.1 ± 9.3	0.403
Female	181 (25.8%)	174 (19.0%)	< 0.001	208 (23.0%)	125 (18.9%)	0.052
Hypertension	509 (72.9%)	721 (78.7%)	0.006	671 (74.5%)	523 (79.5%)	0.021
Diabetes	295 (42.1%)	367 (40.0%)	0.393	370 (40.9%)	264 (40.0%)	0.711
Prior MI	125 (17.9%)	197 (21.5%)	0.074	161 (17.8%)	146 (22.2%)	0.034
Peripheral vascular disease	31 (4.4%)	46 (5.0%)	0.582	34 (3.8%)	42 (6.4%)	0.017
Ejection fraction	61.0 ± 8.0	60.0 ± 8.1	0.005	60.9 ± 8.0	59.7 ± 8.0	0.001
Body mass index	28.3 ± 4.8	29.0 ± 4.8	0.003	28.3 ± 4.6	29.2 ± 5.0	0.001
SAQ-7 Summary Score	72.1 ± 18.8	73.3 ± 19.0	0.158	72.6 ± 19.0	73.2 ± 18.7	0.624
SAQ-7 Angina Frequency Score	79.5 ± 19.7	79.8 ± 20.8	0.334	79.9 ± 20.2	79.5 ± 20.4	0.838
Rose Dyspnea Scale	1.2 ± 1.3	1.2 ± 1.3	0.293	1.2 ± 1.3	1.2 ± 1.3	0.327

No difference in completeness of revascularization by baseline symptoms or QoL

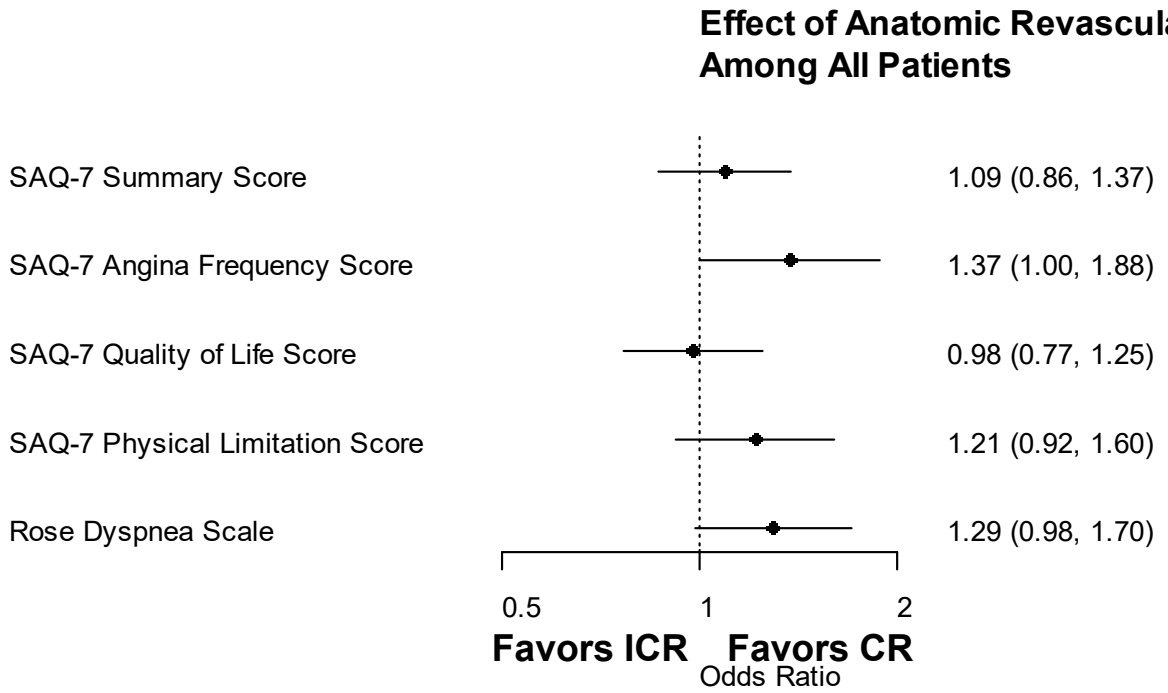
More Complex Anatomy Associated with ICR

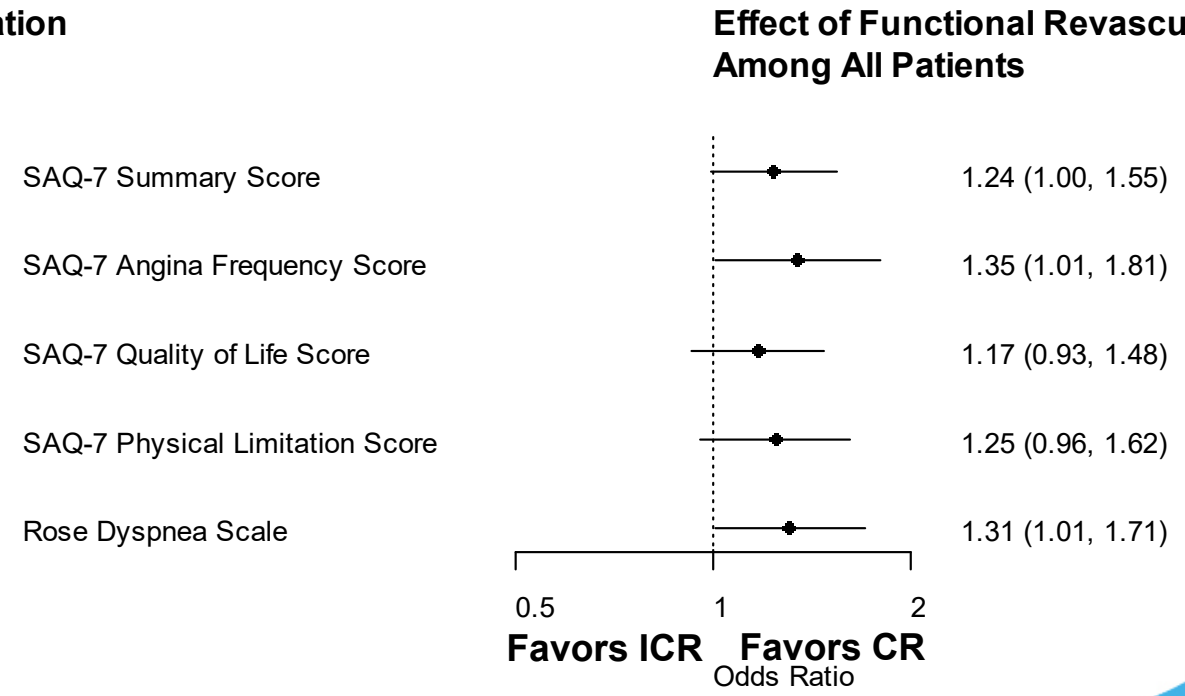
Select Baseline Anatomy and Revascularization Strategy

	Anatomic CR		P-Value	Funtional CR		P-Value
	CR n = 701	ICR n = 918		CR n = 904	ICR n = 660	
# of vessels ≥ 70% (CCTA)			< 0.001			< 0.001
0	48 (8.7%)	25 (3.6%)		48 (6.8%)	16 (3.2%)	
1	171 (31.1%)	178 (25.5%)		220 (31.1%)	122 (24.1%)	
2	82 (14.9%)	144 (20.7%)		111 (15.7%)	110 (21.7%)	
3	39 (7.1%)	114 (16.4%)		61 (8.6%)	92 (18.2%)	
SYNTAX score			< 0.001			< 0.001
<23	577 (82.3%)	499 (54.4%)		697 (77.1%)	329 (49.8%)	
23 to <33	99 (14.1%)	250 (27.2%)		159 (17.6%)	186 (28.2%)	
>= 33	25 (3.6%)	169 (18.4%)		48 (5.3%)	145 (22.0%)	
Number of CTOs			< 0.001			< 0.001
0	475 (67.9%)	411 (44.8%)		587 (65.0%)	249 (37.7%)	
1	194 (27.7%)	401 (43.7%)		275 (30.5%)	315 (47.7%)	
2	30 (4.3%)	87 (9.5%)		39 (4.3%)	78 (11.8%)	
≥3	1 (0.1%)	18 (2.1%)		2 (0.2%)	17 (2.8%)	
First revascularization			< 0.001			< 0.001
PCI	551 (78.6%)	651 (70.9%)		697 (77.1%)	455 (68.9%)	
CABG	150 (21.4%)	267 (29.1%)		207 (22.9%)	205 (31.1%)	

Adjusted QoL Outcomes Favor CR, Particularly with Functional CR

Adjusted Outcomes at 1 year





CR improves health status more than ICR for patients with daily/weekly angina

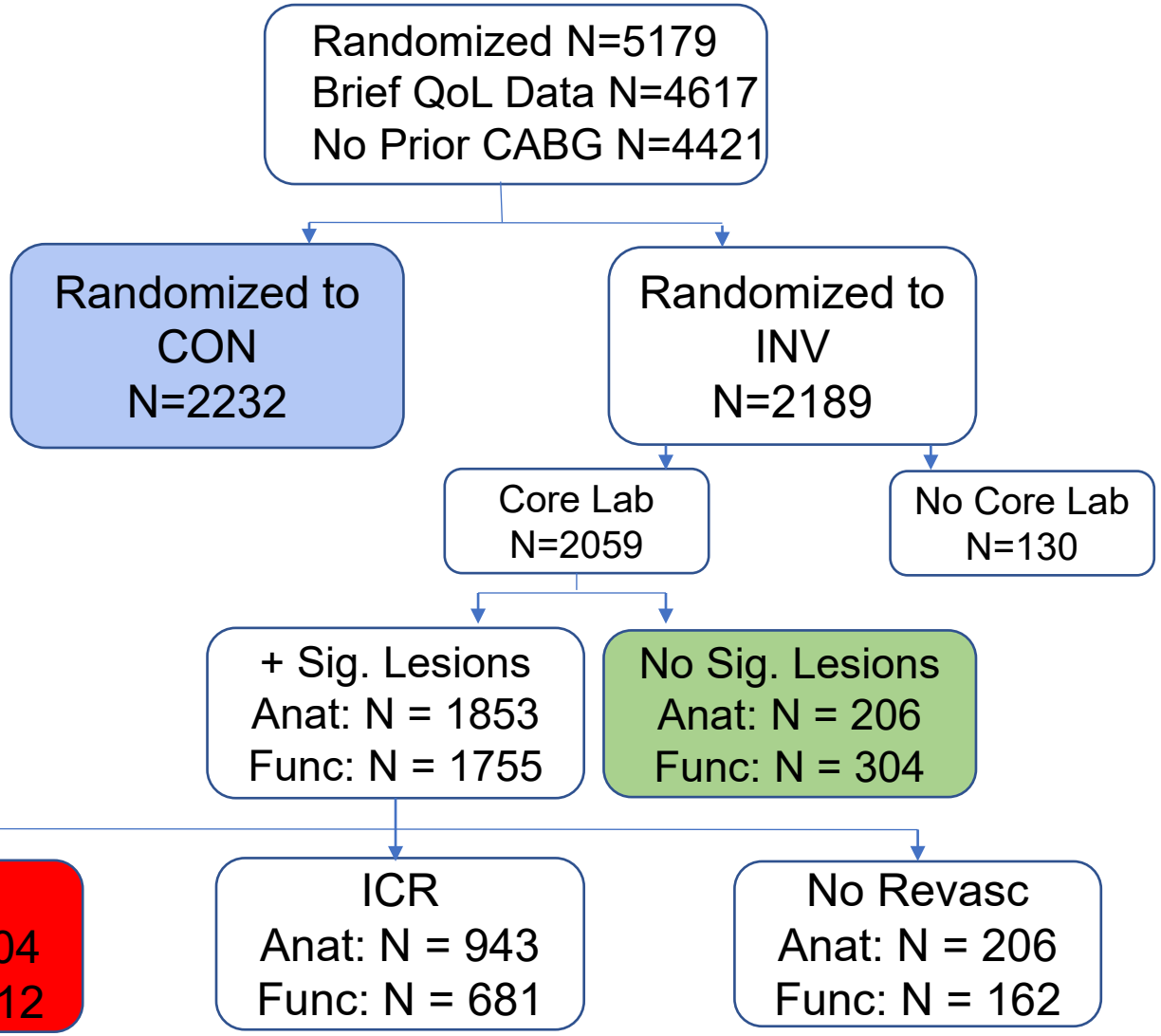
Covariate adjusted odds ratios for better health status-CR vs ICR at 1 year

	Baseline Daily/Weekly Angina	Baseline Monthly Angina	Baseline No Angina	Interaction P-value
Anatomic CR vs ICR				
SAQ-7 Summary Score	**1.62 (1.07, 2.44)**	0.89 (0.66, 1.19)	1.13 (0.78, 1.63)	0.04
SAQ-7 Angina Frequency Score	**2.20 (1.28, 3.77)**	1.03 (0.70, 1.52)	1.44 (0.80, 2.61)	0.04
Functional CR vs ICR				
SAQ-7 Summary Score	**1.55 (1.03, 2.34)**	1.18 (0.88, 1.59)	1.14 (0.80, 1.63)	0.44
SAQ-7 Angina Frequency Score	**2.01 (1.22, 3.31)**	1.13 (0.76, 1.69)	1.19 (0.67, 2.10)	0.14

No association of CR benefit with ischemia burden or number of CTOs

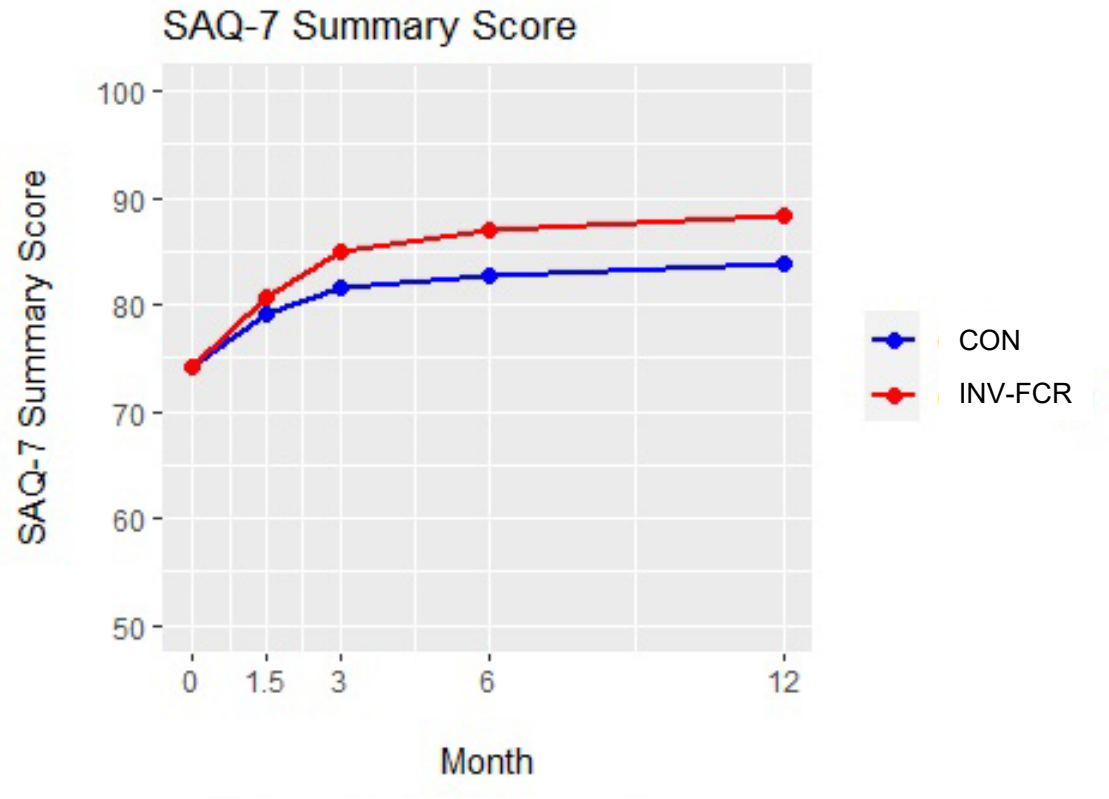
Objective 2: Invasive-CR vs Conservative

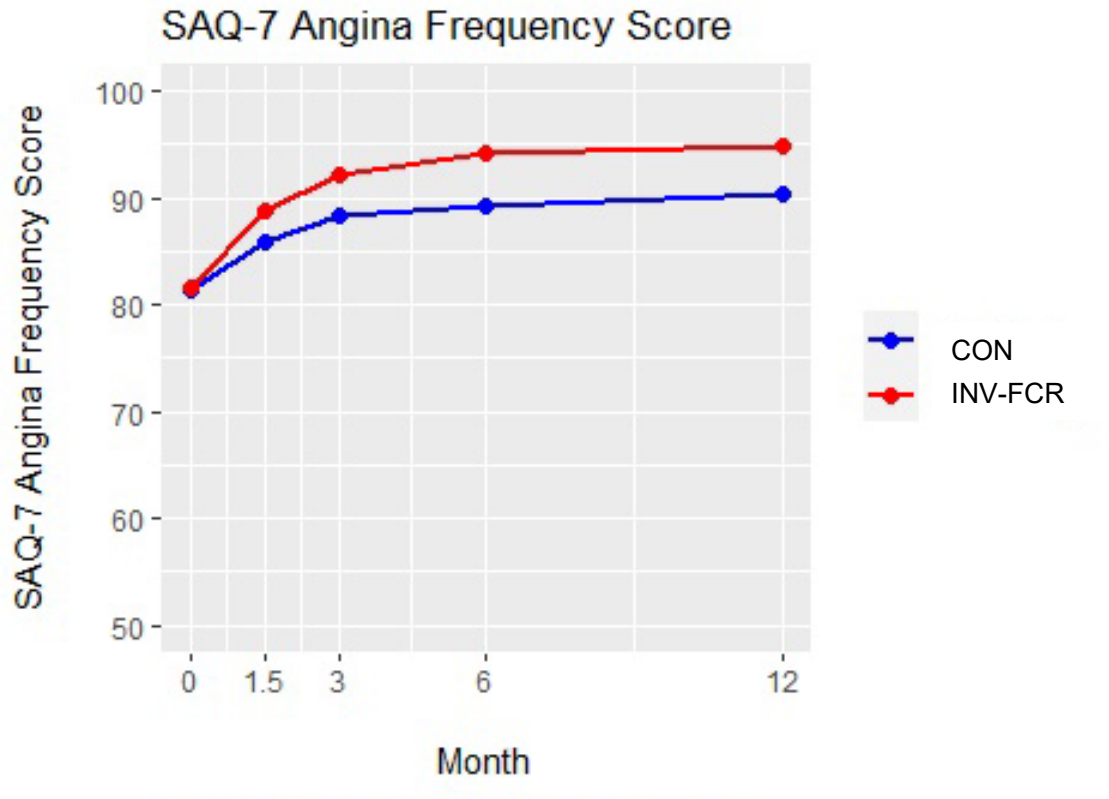
Patient Flow



Objective 2: INV-FCR vs CON

Propensity weighted SAQ scores





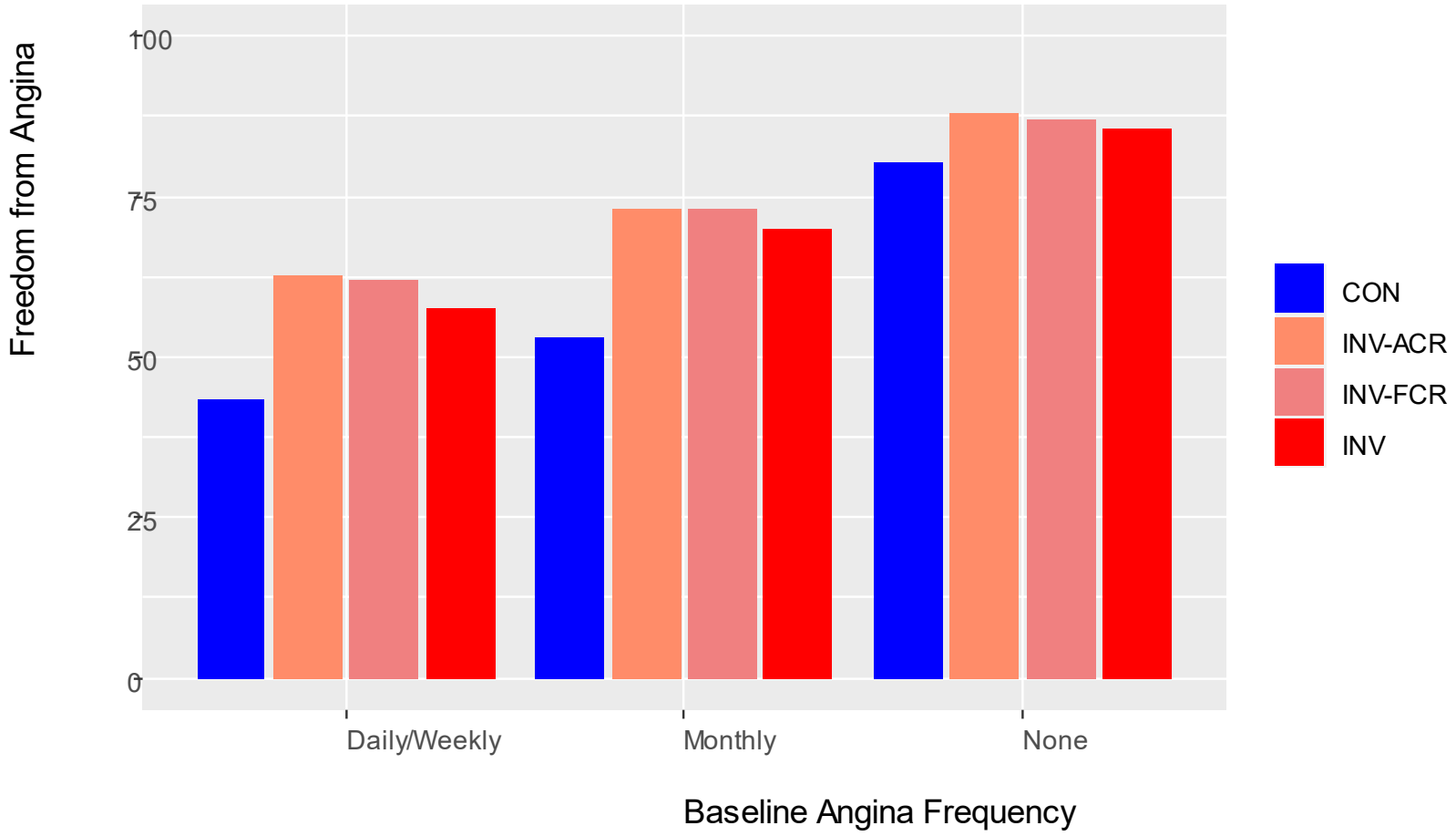
INV-CR vs CON vs. Randomized ISCHEMIA

Adjusted mean difference in QoL scores at 1 year

	ISCHEMIA CR Substudy Analysis		ISCHEMIA Trial*
	INV-ACR vs. CON	INV-FCR vs. CON	INV vs. CON
SAQ-7 Summary Score	4.3 (3.2, 5.6)	4.3 (3.1, 5.5)	3.7 (2.9, 4.6)
SAQ-7 Angina Frequency Score	4.3 (3.3, 5.2)	4.7 (3.6, 5.6)	3.7 (2.8, 4.6)
SAQ-7 Quality of Life Score	5.6 (3.8, 7.6)	5.9 (3.7, 7.8)	4.6 (3.3, 6.0)
SAQ-7 Physical Limitation Score	3.0 (1.4, 4.7)	3.3 (1.8, 4.8)	2.6 (1.5, 3.8)
Rose Dyspnea Scale	-0.2 (-0.3, -0.1)	-0.2 (-0.3, -0.1)	-0.1 (-0.2, -0.1)

*Excluded: Pts with prior CABG

Freedom from Angina Highest in INV-CR



Benefits differ by Baseline Angina, but Not by Ischemia

Baseline Angina

	Daily/Weekly Angina	Monthly Angina	No Angina	Interaction P-value
INV-FCR vs CON				
SAQ-7 Summary Score	7.0 (4.3, 9.9)	5.4 (3.5, 7.1)	1.8 (0.3, 3.4)	<0.001
SAQ-7 Angina Frequency Score	7.7 (4.8, 10.8)	4.9 (3.5, 6.3)	1.9 (0.9, 3.0)	<0.001
Freedom from angina (OR)	2.31 (1.55, 3.44)	2.35 (1.65, 3.14)	1.62 (1.15, 2.26)	<0.001

Baseline Ischemia

	No-Mild Ischemia	Moderate Ischemia	Severe Ischemia	Interaction P-value
INV-FCR vs CON				
SAQ-7 Summary Score	3.9 (1.2, 6.6)	4.9 (3.1, 6.9)	4.4 (2.4, 6.0)	0.83
SAQ-7 Angina Frequency Score	2.8 (-0.0, 5.5)	4.8 (3.1, 6.6)	4.7 (3.5, 5.9)	0.43
Freedom from angina (OR)	1.69 (1.13, 2.59)	2.17 (1.58, 2.92)	2.36 (1.69, 3.14)	0.41

Limitations

- Observational comparison, so association cannot be equated with causality
  - Methods to match/adjust used 24 prospectively-collected, clinical and angiographic factors
  - However, we acknowledge likely residual confounding

- No sham group—cannot exclude placebo effect--however, benefit in QoL comparable to the sham-controlled ORBITA Trial

Conclusions (1)

- CR is associated with a greater improvement in angina-related quality of life than ICR, particularly in patients with baseline weekly/daily angina

- Functional CR is at least as effective as anatomic CR in improving angina-related quality of life

Conclusions (2)

- Invasive management achieving CR improves angina-related quality of life more than conservative management, with greater benefits in the patients with more angina.

- Stress-induced ischemia burden on non-invasive testing and presence of CTOs do not identify patients who benefit more or less from CR.

Clinical Implications

These results suggest that, for patients with chronic coronary disease and angina who are being managed invasively, the safe achievement of CR will optimize quality of life.

Thank you…..

- John Spertus, Gregg Stone
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