

The slide features a solid red background. On the left side, there is a vertical purple bar. The title text is centered on the red background.

Impact Of Complete Revascularization in the ISCHEMIA TRIAL

BACKGROUND

- Despite advances in CABG and PCI, reduced rates of CV death and MI have not been demonstrated in most randomized trials of revascularization compared with medical therapy in chronic coronary disease (CCD).
- In the ISCHEMIA trial (*International Study of Comparative Health Effectiveness with Medical and Invasive Approaches*), 5,179 patients with CCD and at least moderate ischemia were randomized to an
 - initial INV strategy (angiography and revascularization with PCI or CABG as appropriate per site discretion) + medical therapy vs
 - an initial CON strategy of medical therapy alone with angiography and revascularization reserved for medical therapy failure.

coronary artery bypass graft surgery (CABG) | percutaneous coronary intervention (PCI) | myocardial infarction (MI) | chronic coronary disease (CCD).

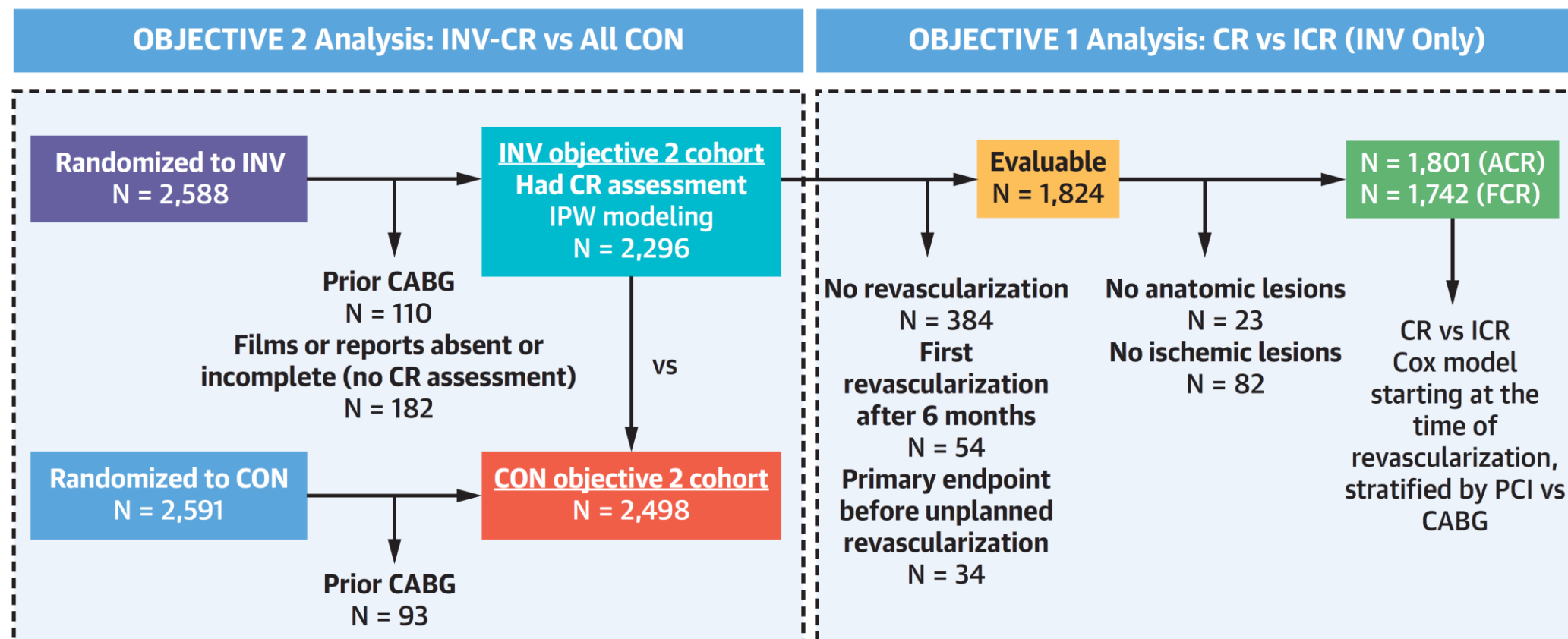
Stone GW et al. J Am Coll Cardiol. 2023 Jul 11:S0735-1097(23)06031-X. doi: 10.1016/j.jacc.2023.06.015. Epub ahead of print.

OBJECTIVES

- Among patients with chronic coronary disease without prior coronary artery bypass grafting randomized to INV vs CON management in the ISCHEMIA trial, examined the following:
 - 1) the outcomes of ACR and FCR compared with incomplete revascularization; and
 - 2) the potential impact of achieving CR in all INV patients compared with CON management.

anatomic complete revascularization (ACR) | functional (ischemic) complete revascularization (FCR)

DERIVATION OF THE PATIENT COHORTS



For Objective 1 (right), among invasive treatment strategy (INV)-assigned patients, the impact of achieving anatomic complete revascularization (ACR) and functional complete revascularization (FCR) vs incomplete revascularization (ICR) was assessed in 1,801 and 1,742 patients, respectively.

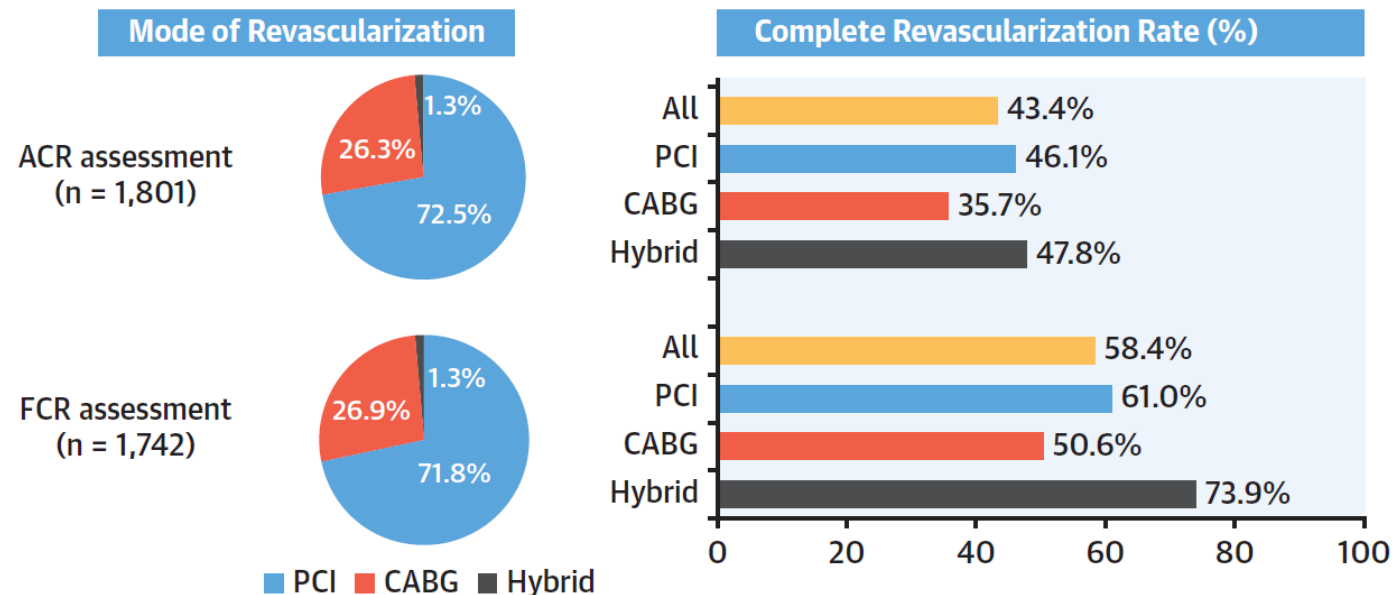
For Objective 2 (left), IPW with complete revascularization (CR) as a time-dependent variable was used to estimate the hypothetical ideal treatment effect for 2,296 INV-assigned patients without prior coronary artery bypass grafting (CABG) in whom the completeness of revascularization could be assessed by the angiographic core laboratory and who received CR at the time of randomization, compared with conservative treatment strategy (CON) management in 2,498 patients without prior CABG. IPW $\frac{1}{4}$ inverse probability weighting

METHODS

- ACR and FCR in the INV group were assessed at an independent core laboratory. Multivariable-adjusted outcomes of CR were examined in INV patients.
- Inverse probability weighted modeling was then performed to estimate the treatment effect had CR been achieved in all INV patients compared with CON management

RESULTS

- Among 1,801 INV patients evaluable for ACR assessment, PCI, CABG, and hybrid revascularization were performed in 1,305 (72.5%), 473 (26.3%), and 23 (1.3%), respectively.
- ACR was achieved in 781 (43.4%) patients. Among 1,742 INV patients evaluable for FCR assessment, PCI, CABG, and hybrid revascularization were performed in 1,251 (71.8%), 468 (26.9%), and 23 (1.3%), respectively. FCR was achieved in 1,017 (58.4%) patients.

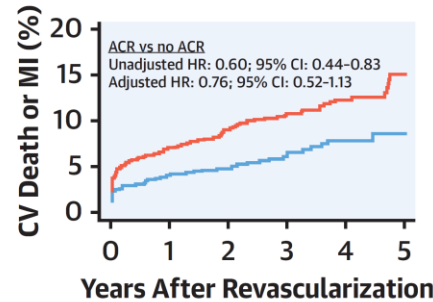


IMPACT OF CR COMPARED WITH ICR IN INV.

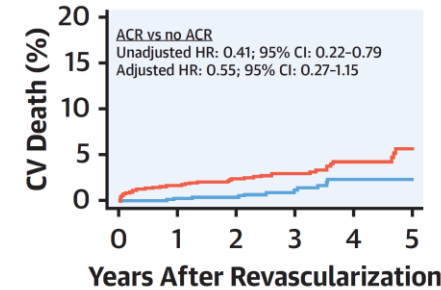
- In unadjusted analyses, both ACR and FCR compared with ICR were strongly associated with reduced rates of cardiovascular death and MI during follow-up.
- After accounting for differences in clinical and anatomic characteristics in patients with CR vs ICR, the benefits of both ACR and FCR were attenuated.
- These results were consistent using the secondary MI definition

Relationship Between Complete Revascularization and Outcomes With Invasive Management

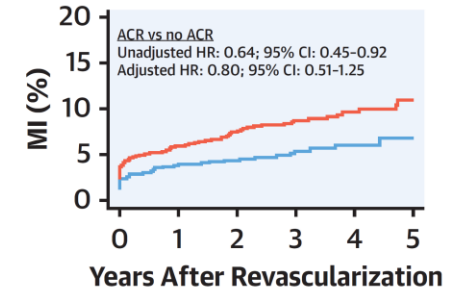
Outcomes According to Anatomic Complete Revascularization



No. at risk						
ACR	781	739	589	370	179	67
Not ACR	1,020	936	723	504	293	110

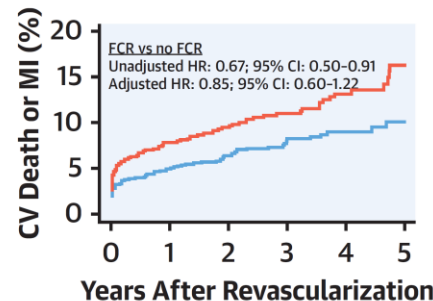


No. at risk						
ACR	781	772	618	396	192	72
Not ACR	1,020	994	779	557	328	124

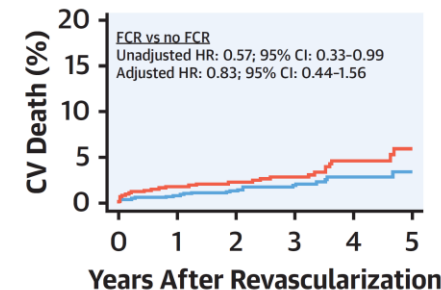


No. at risk						
ACR	781	739	589	370	179	67
Not ACR	1,020	934	723	504	293	110

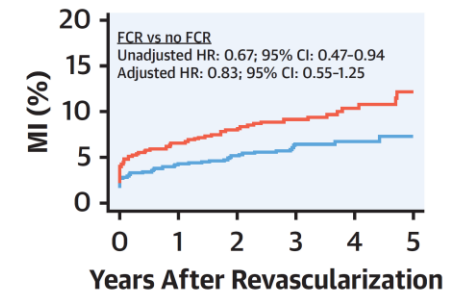
Outcomes According to Functional Complete Revascularization



No. at risk						
FCR	1,017	955	748	484	246	91
Not FCR	725	661	516	361	212	83



No. at risk						
FCR	1,017	1,001	792	524	268	97
Not FCR	725	706	556	399	237	96

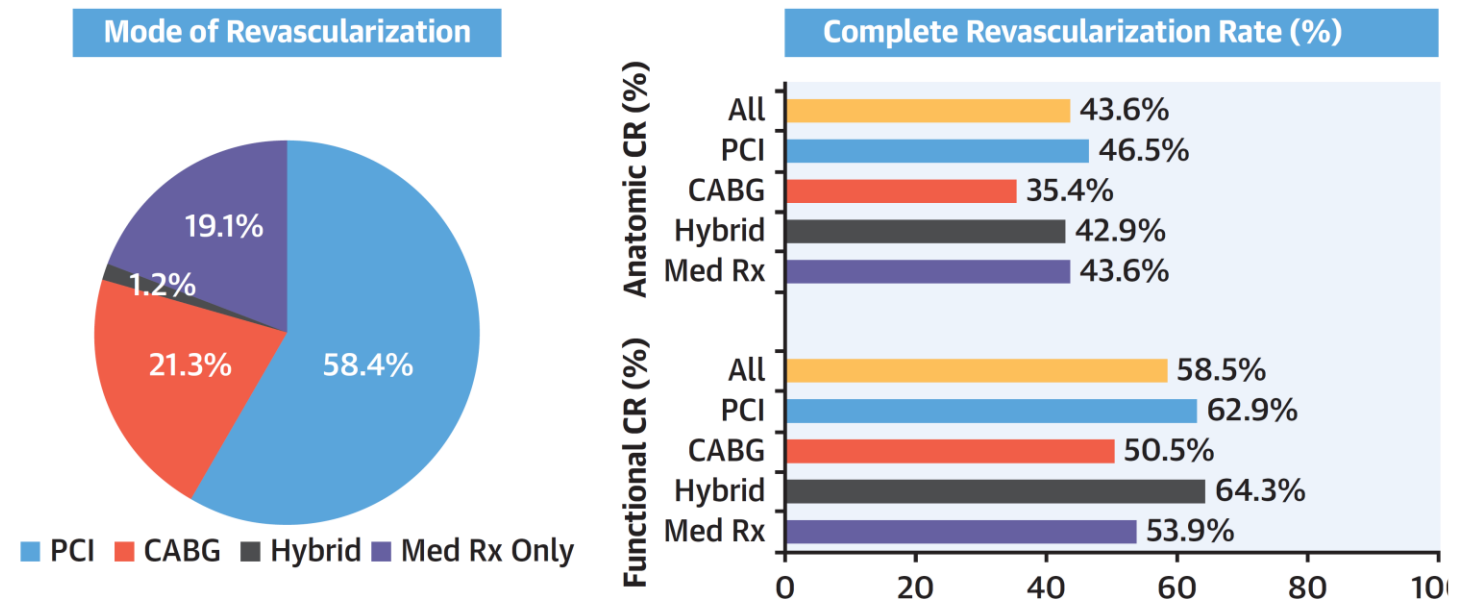


No. at risk						
FCR	1,017	954	748	484	246	91
Not FCR	725	660	516	361	212	83

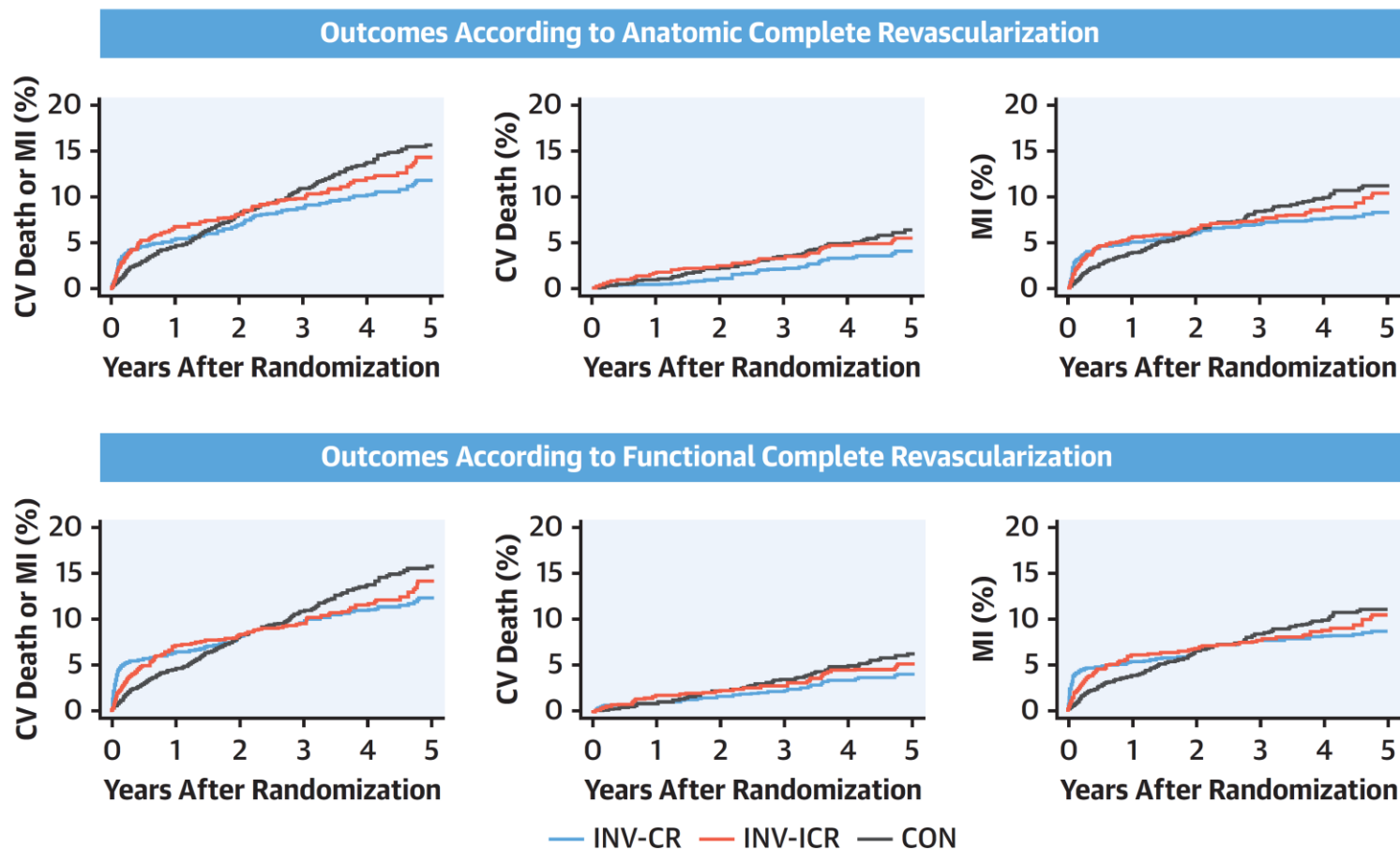
— Complete Revascularization — Incomplete Revascularization

MODE AND COMPLETENESS OF REVASCULARIZATION IN ALL INVASIVE TREATMENT STRATEGY PATIENTS

- Among 2,296 INV patients evaluable for CR assessment, PCI, CABG, and hybrid revascularization were performed in 1,341 (58.4%), 489 (21.3%), and 28 (1.2%) respectively.
- 438 (19.1%) of patients were treated medically without revascularization within 6 months.
- ACR and FCR were achieved in 1,000 (43.6%) and 1,344 (58.5%) patients, respectively



(Left) The type of first revascularization procedure performed or treatment with medical therapy alone in 2,296 patients within 6 months after randomization to an invasive management strategy. (Right) Rates of anatomic CR (top) and functional CR (bottom) achieved in all patients and by treatment modality. In these unadjusted analyses, CR was achieved more frequently with PCI than CABG

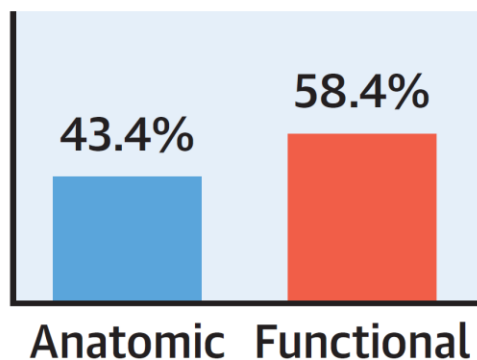


**OUTCOMES AFTER
COMPLETE AND
INCOMPLETE
REVASCULARIZATION
COMPARED WITH
CONSERVATIVE
MANAGEMENT**

IMPACT OF COMPLETE REVASCULARIZATION IN THE ISCHEMIA TRIAL

OBJECTIVE 1: Among 1,824 INV-Assigned Patients in Whom Revascularization was Performed

Achievement of CR



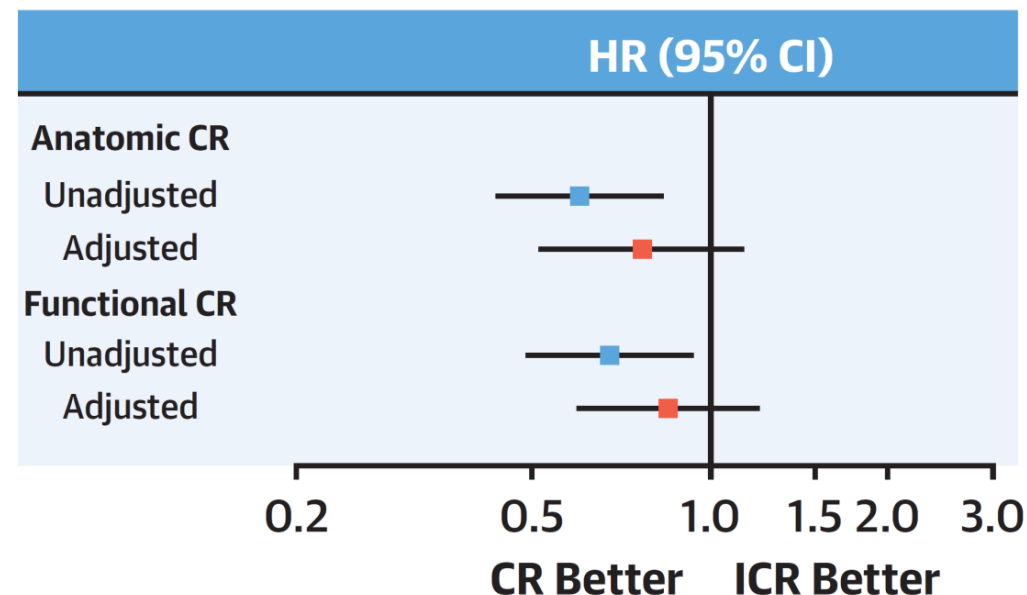
Independent Predictors of CR

Clinical: Diabetes, low BMI

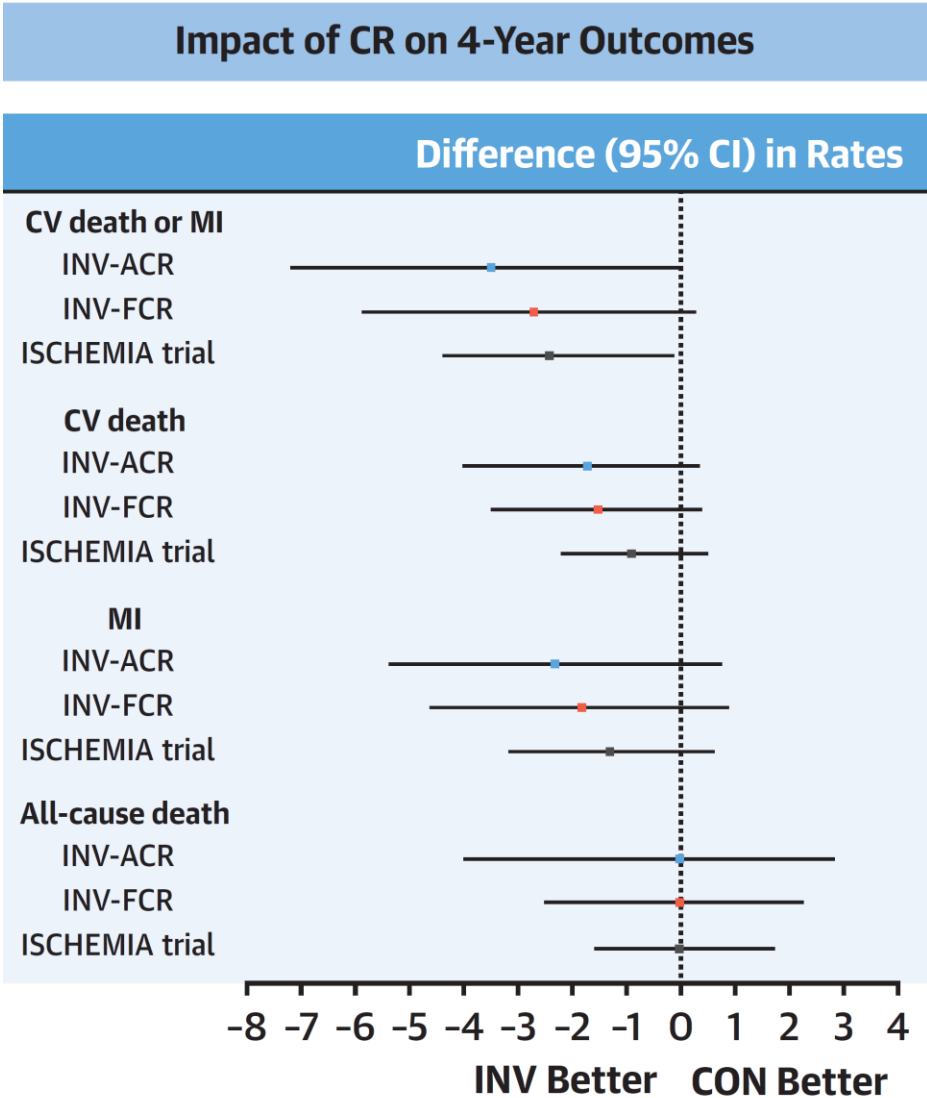
Angiographic: Low anatomic complexity (low SYNTAX score, no CTOs), LM, or PLAD disease

Modality: CABG (vs PCI)

Impact of CR on 4-Year CV Death or MI



**OBJECTIVE 2: Among 2,296 INV-Assigned Patients
Compared With 2,498 CON-Assigned Patients**



**IMPACT OF
COMPLETE
REVASCULARIZATION
IN THE ISCHEMIA
TRIAL**

CONCLUSION

CR was achieved in approximately one-half of INV assigned patients in the ISCHEMIA trial.

CR (especially ACR) was strongly associated with freedom from cardiovascular death or MI in unadjusted analyses (as in most prior reports), but this effect was lessened after accounting for the confounding effects of the extent and complexity of CAD.

The benefits of FCR were directionally similar to those of ACR but less pronounced.

Had ACR been achieved in all randomized INV patients, the composite rate of cardiovascular death or MI may have been reduced by ~3.5% over 4 years compared with CON management, an ~1% absolute improvement (number needed-to-treat ~100) compared with the observed outcomes in the overall ISCHEMIA trial, which is a modest but desirable goal if CR may be safely achieved.

CLINICAL TAKEAWAYS

Findings from this prespecified analysis from the landmark ISCHEMIA trial show that an invasive strategy led to complete revascularization in only 50% of patients.

When complete revascularization is achieved, it is associated with greater health status improvement than incomplete revascularization.

Invasive strategy (complete or incomplete revascularization) was associated with greater health status gain than conservative management.

The benefit of complete revascularization was largely seen among patients with daily or weekly angina and minimally among patients with monthly angina or asymptomatic patients.



Thank you