

Implications of the ISCHEMIA Trial on Patient Selection for CTO-PCI

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ISCHEMIA Trial: Summary

- 5179 patients randomized to INV vs. CON
 - *Largest treatment strategy trial of SIHD*
- Enrolled high-risk subset
 - *54% severe ischemia; 76% with multivessel CAD; 47% with proximal LAD disease (CCTA)*
- Cath and Revascularization
 - *Invasive strategy: 80% revascularized (74% PCI/26% CABG)*
 - *Conservative strategy: 28% cath; 23% revasc at 4-years*
- Medication Therapy
 - *95% statins; 66% high intensity statin; LDL 64 mg/dl; SBP 129 mm Hg*

Which Patients were Not Enrolled in ISCHEMIA?

- ACS within 2 months
- EF < 35%
- NYHA Class III-IV HF
- Unacceptable angina despite medical therapy
- PCI or CABG within 1 year
- Severe left main disease

ISCHEMIA Trial

Summary of Major Findings

- No difference in primary or major secondary endpoint
- To improve survival
 - *No improvement in survival compared with MT*
 - *INV-Reduction (0.3%/year) in cardiac death at long term follow-up*
- To prevent other cardiovascular events
 - *INV Reduces spontaneous MI, unstable angina and lowers CV stays*
- To improve quality of life
 - *INV results in faster and more durable relief of angina in symptomatic patients*

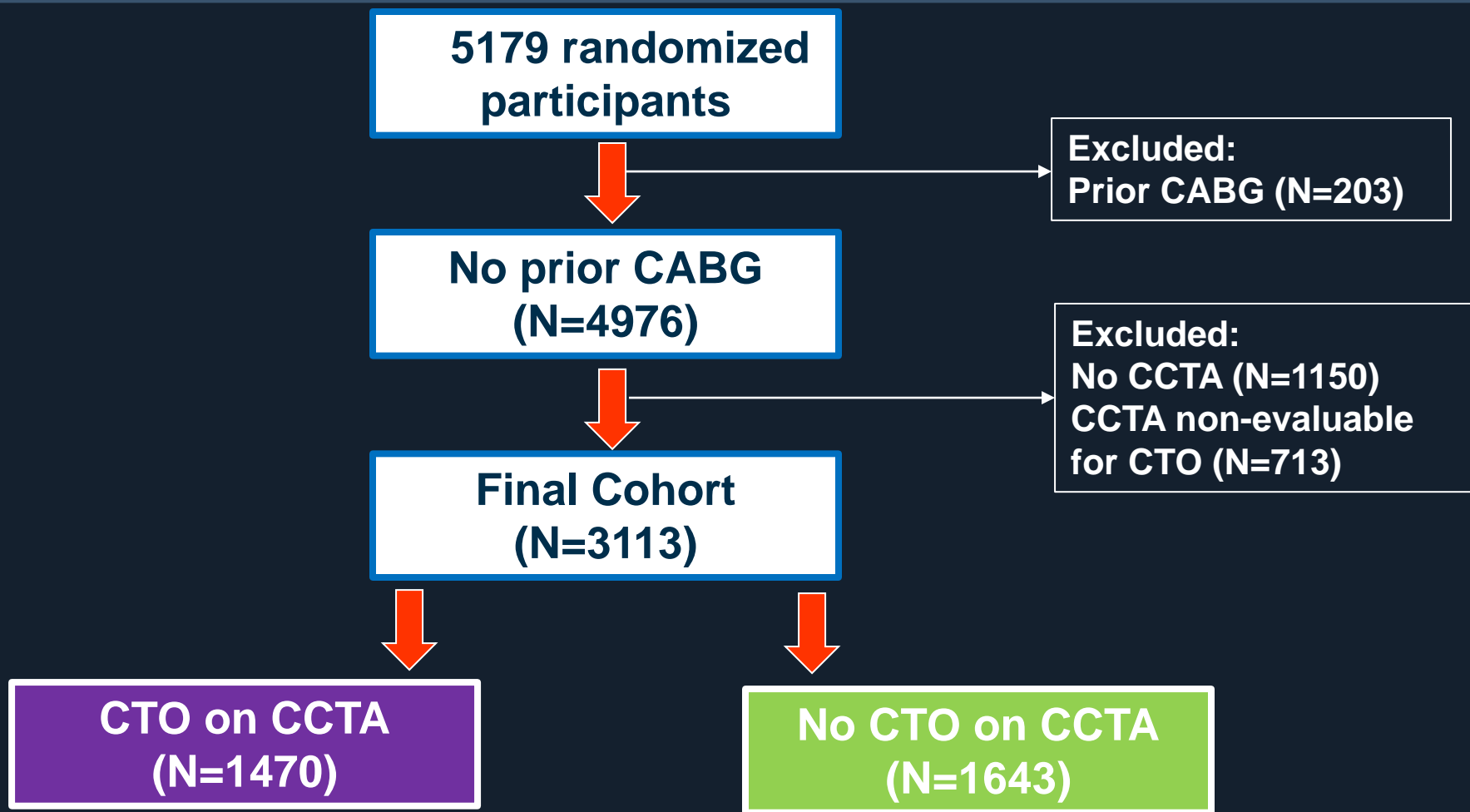
Randomized Trials of CTO Revascularization vs. OMT

Primary Endpoint

- **EXPLORE**: 304 patients with STEMI and CTO
 - CMRI LVEF and LVEDV at 4 months: **No difference**
- **EURO-CTO**: 396 patients with CTO (planned 600)
 - SAQ Angina frequency and QoL at 12 m: **PCI better**
- **DECISION CTO**: 834 patients with CTO (planned 1284)
 - Death, MI, stroke, or any repeat revascularization at 5 years: **No difference**
 - SAQ angina frequency and QoL: **No difference**

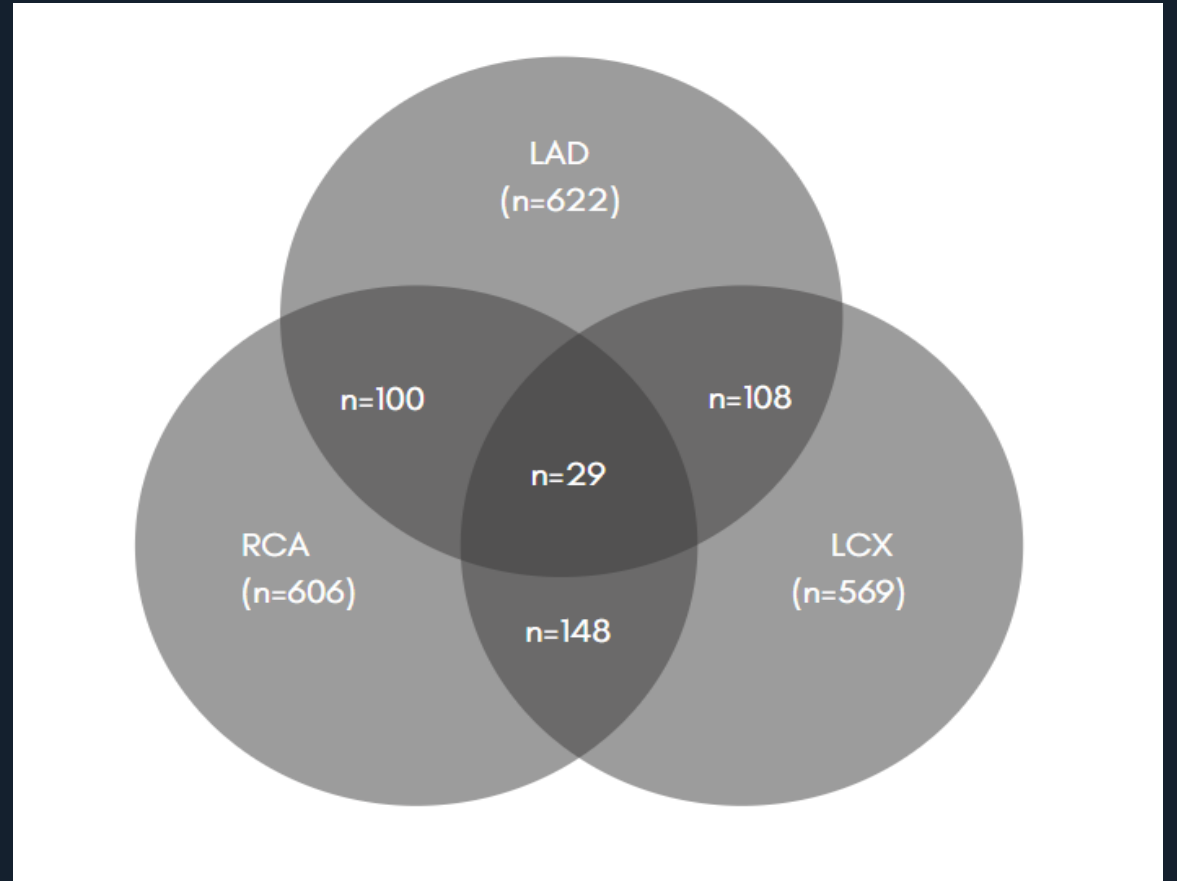
ISCHEMIA CTO Substudy

Study Population



Number and Location of CTOs

- Total of 1797 CTOs in 1470 patients
- The mean number of CTO was 1.22 (SE 0.46)



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Baseline Characteristics

| | CTO (N=1470) | No CTO (N=1643) | P-Value |
|-------------------------------------|-----------------|--------------------|---------|
| Demographics | | | |
| Age (Q1, Q3) | 62 (56, 69) | 64 (57, 70) | <0.01 |
| Female sex | 17% | 21% | 0.01 |
| Clinical history | | | |
| Hypertension | 69% | 68% | 0.90 |
| Diabetes | 41% | 41% | 0.72 |
| Prior MI | 19% | 13% | <0.01 |
| Prior Heart Failure | 4% | 2% | <0.01 |
| Angina History | 89% | 91% | 0.03 |
| New onset angina within 3 months | 17% | 23% | <0.01 |

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Stress Test Characteristics

| | CTO (N=1470) | No CTO (N=1643) | P-Value |
|--------------------------------|-----------------|--------------------|---------|
| Stress imaging overall | | | <0.01 |
| Severe | 537/1040 (52%) | 522/1051 (50%) | - |
| Moderate | 422/1040 (41%) | 401/1051 (38%) | - |
| Mild/None | 81/1040 (8%) | 128/1051 (12%) | - |
| Exercise tolerance test | | | 0.30 |
| Severe | 368/410 (90%) | 492/567 (87%) | - |
| Moderate | 30/410 (7%) | 49/567 (9%) | - |
| Mild/None | 12/410 (3%) | 26/567 (5%) | - |

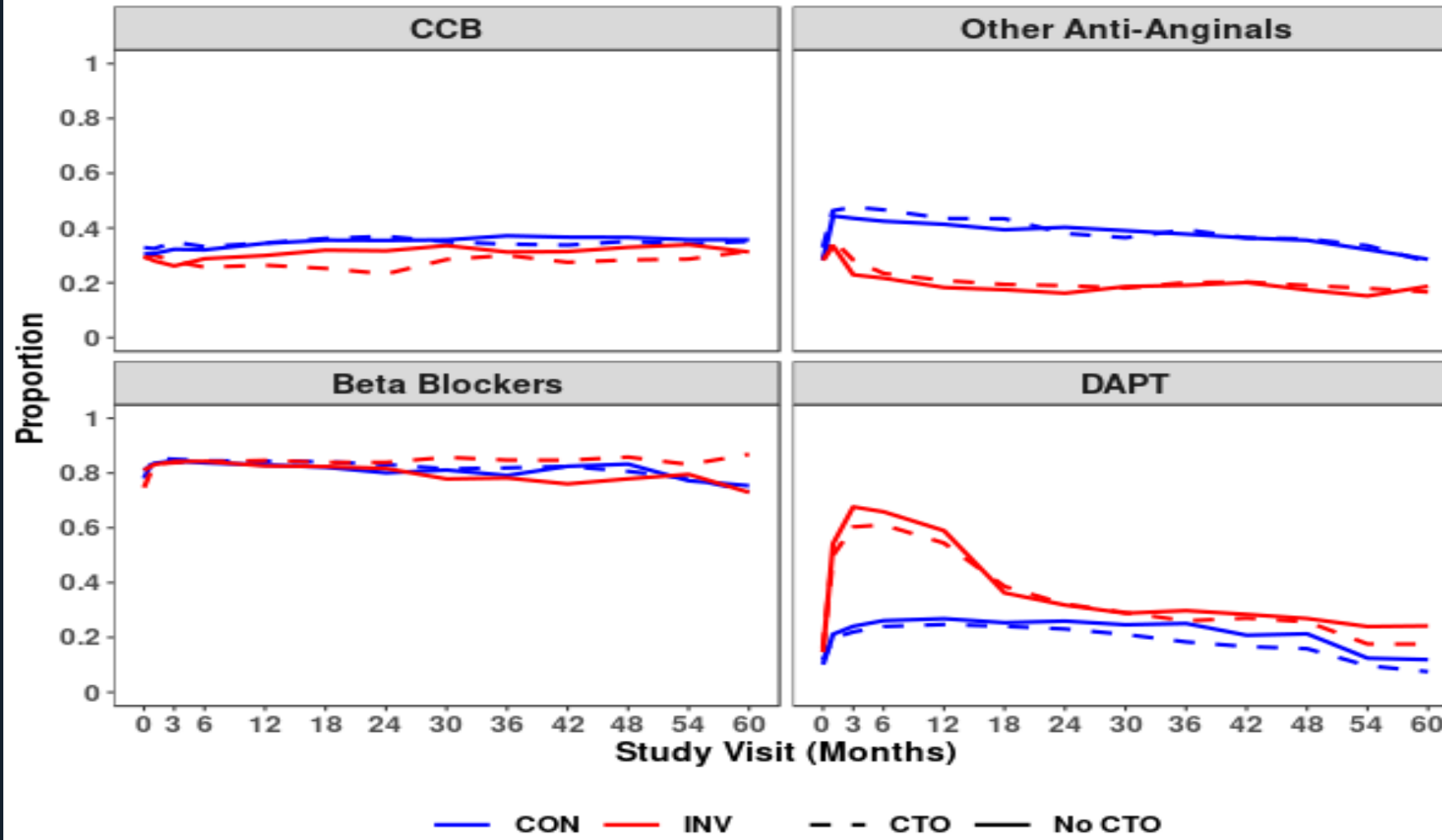
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CCTA Characteristics

| | CTO (N=1470) | No CTO (N=1643) | P-Value |
|---|-------------------|--------------------|---------|
| Number of diseased vessels ($\geq 50\%$ stenosis) | | | <0.01 |
| 1 | 14.4% (181/1254) | 25.1% (316/1261) | - |
| 2 | 30.1% (378/1254) | 33.1% (418/1261) | - |
| 3 | 55.4% (695/1254) | 41.8% (527/1261) | - |
| LAD | 84.2% (1238/1470) | 84.5% (1389/1643) | 0.84 |
| Proximal LAD disease | 46.0% (676/1470) | 46.4% (762/1643) | 0.85 |
| RCA | 72.2% (1061/1470) | 57.5% (944/1643) | <0.01 |
| LCX | 72.9% (1071/1470) | 59.0% (969/1643) | <0.01 |

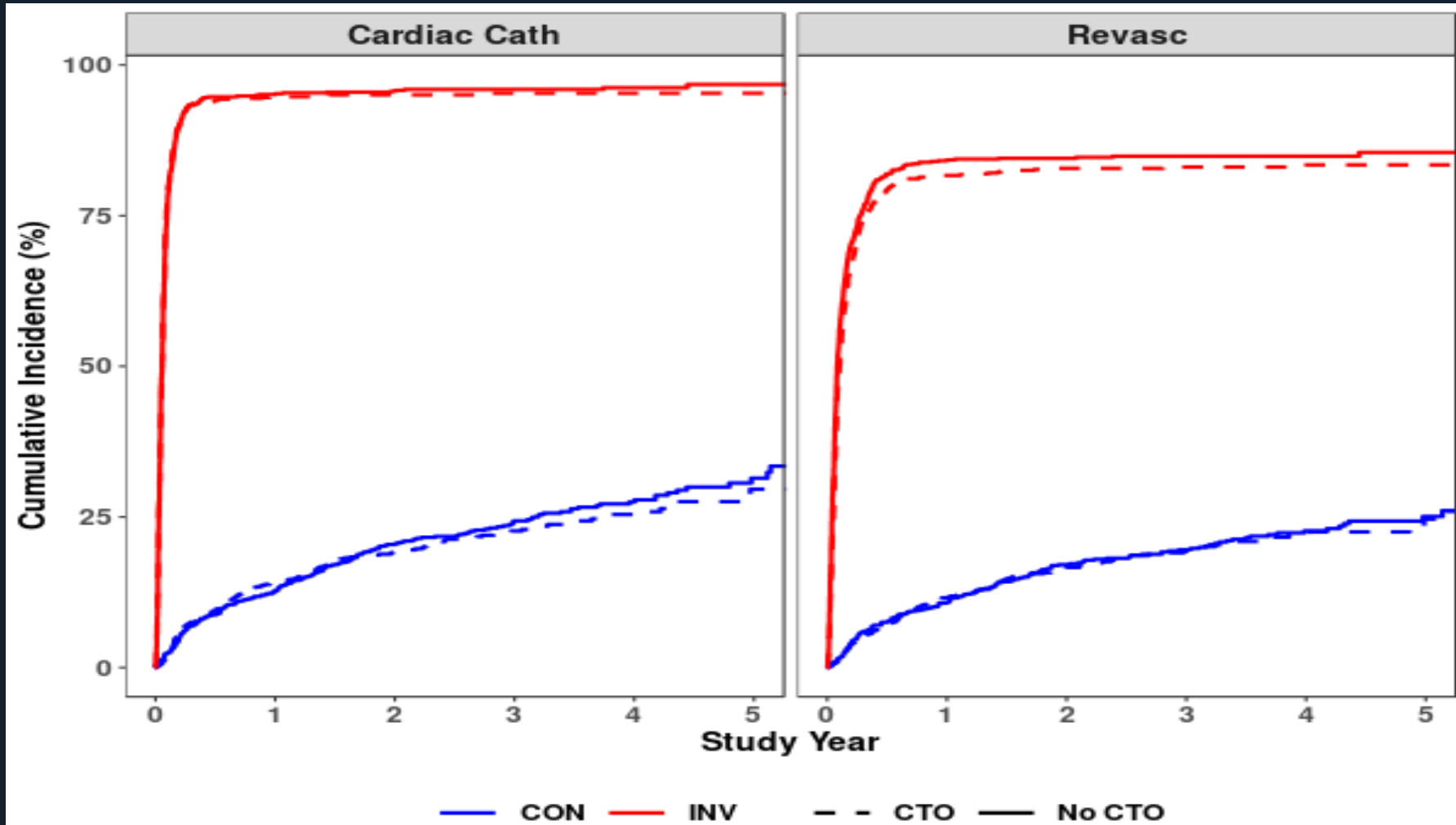
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Medication Use by CTO Status



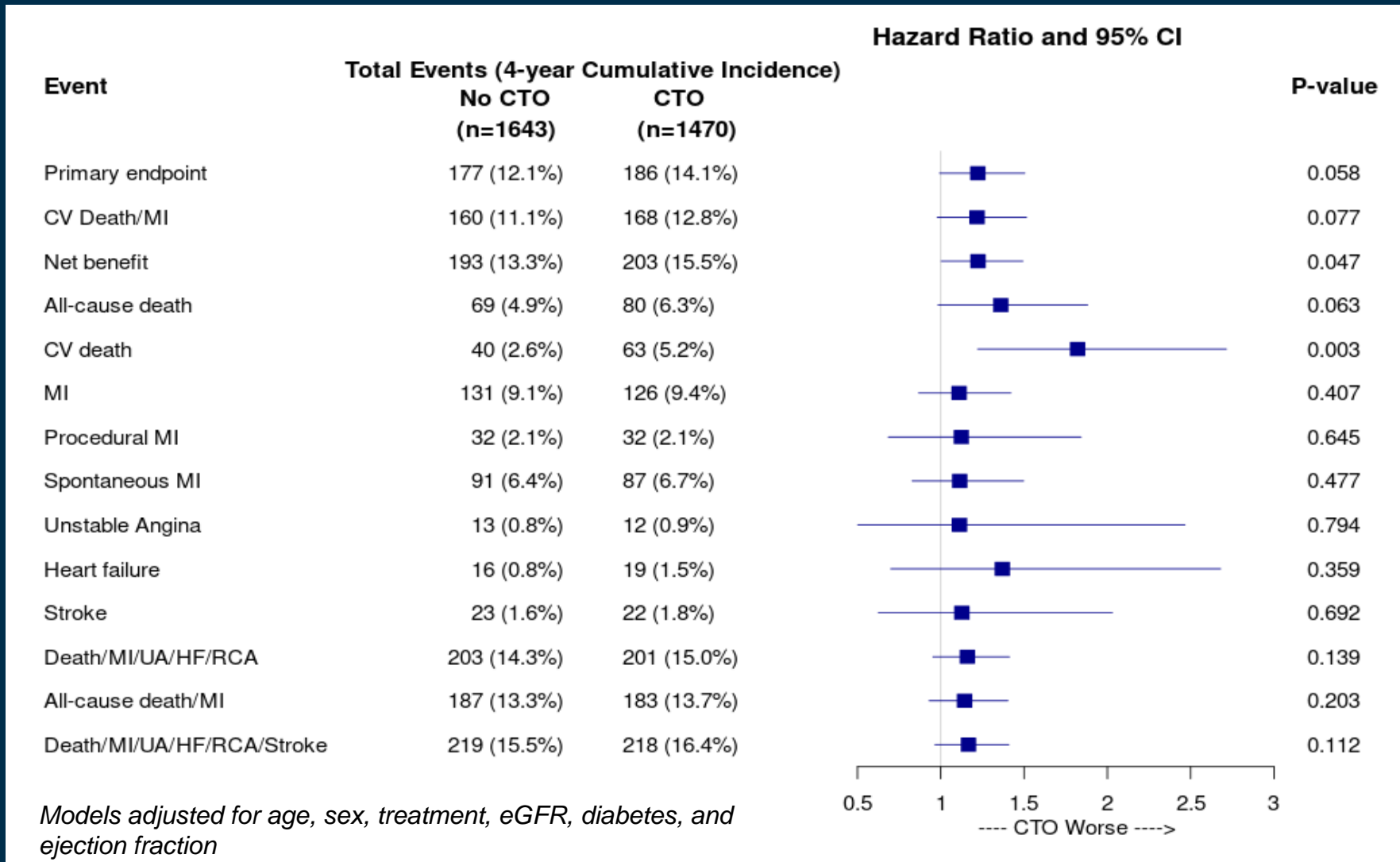
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Cardiac Cath/Revasc by CTO Status and Randomized Group



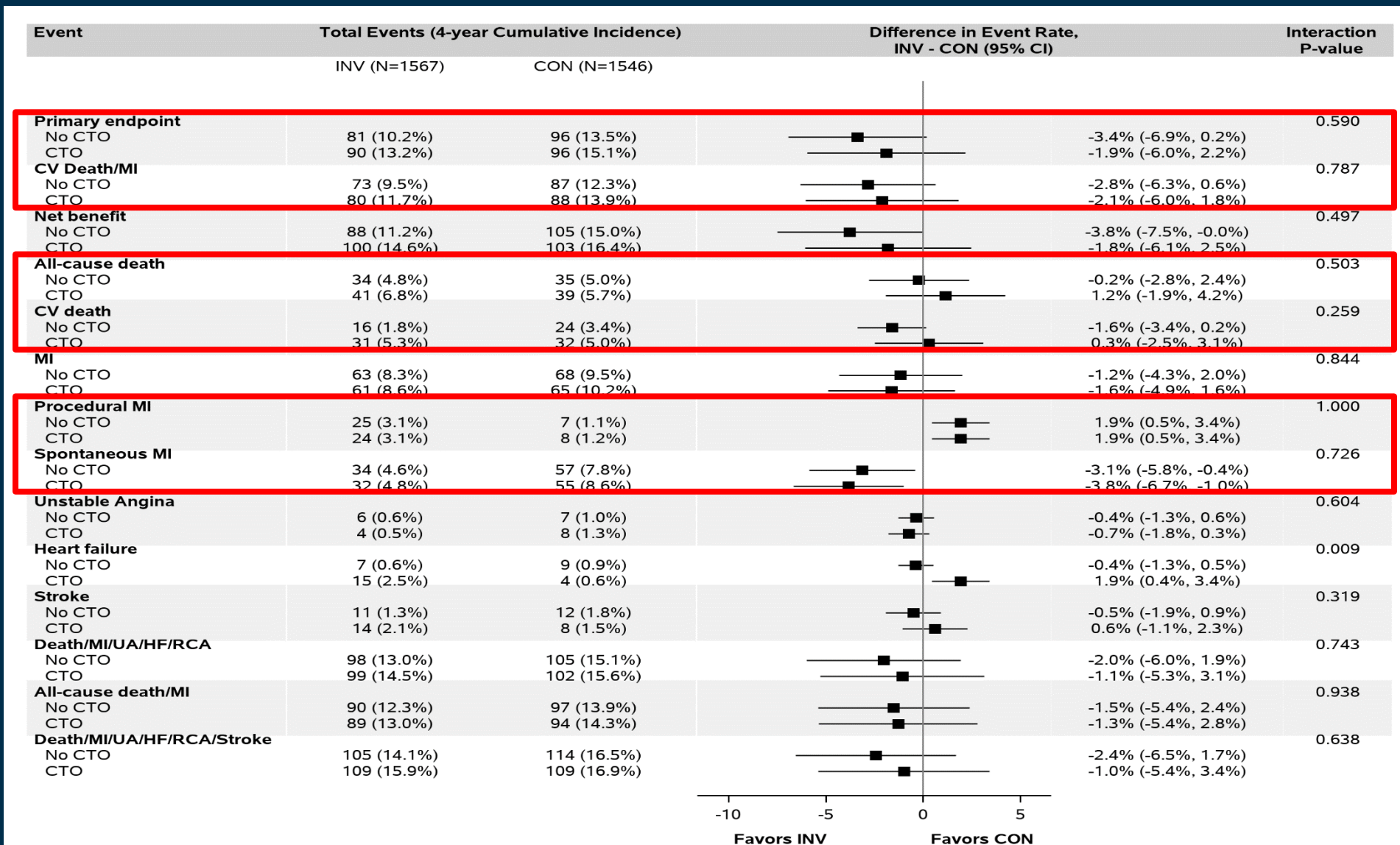
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Aggregate Outcome based on CTO Status



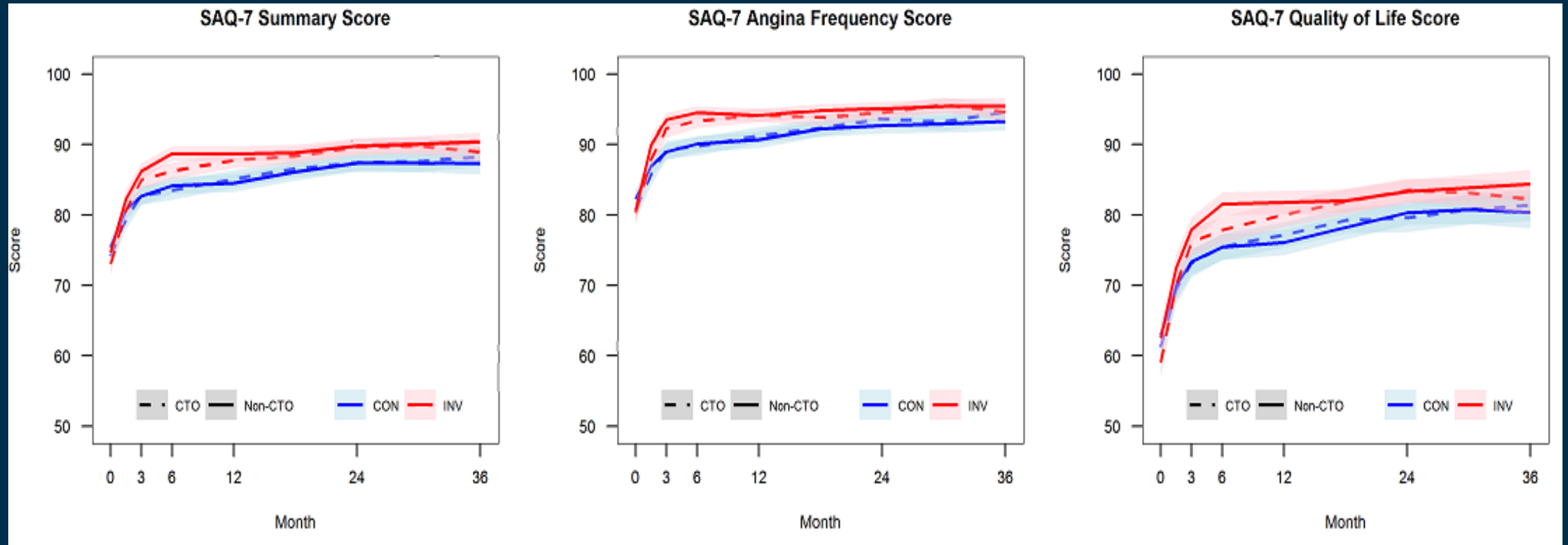
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Outcomes by Treatment Group and CTO Status



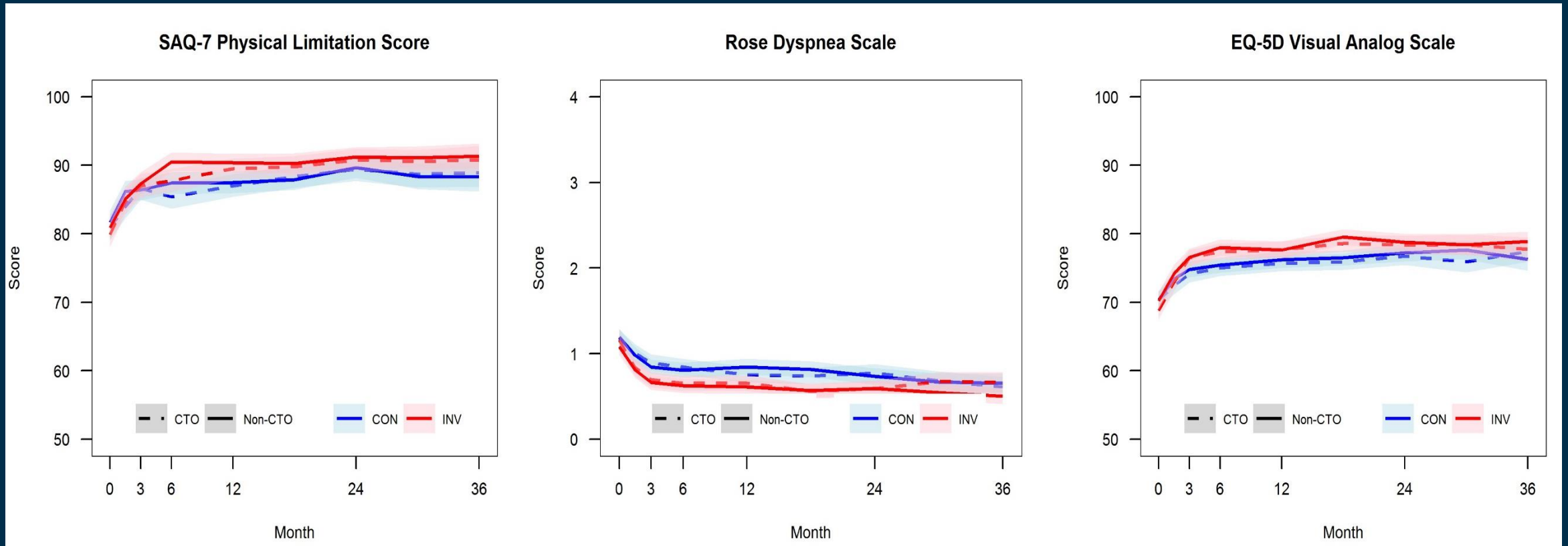
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Quality of Life- Treatment Effect



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Quality of Life- Treatment Effect



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Study Limitations

- Analysis is based on intention to treat
 - As treated (based on actual status of CTO revascularization) is in progress
 - The determination of CTO was based on coronary CTA
 - Patients who were very symptomatic, or dissatisfied with medical therapy were excluded and the results do not apply to such patients

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Summary

- Almost 1 in 2 randomized patients in ISCHEMIA who underwent coronary CTA had at least 1 CTO. *Sample size more than EURO CTO and DECISION CTO combined together.*
- Patients with CTO when compared to no-CTO in ISCHEMIA had:
 - Greater amount of ischemia
 - Worse prognosis with higher risk of cardiovascular events
 - Similar quality of life including angina-specific quality of life

Implications of the ISCHEMIA Trial on Patient Selection for CTO-PCI

- Aggressive GDMT for all patients
- Consider invasive strategy and revascularization
 - To improve angina related health status in symptomatic patients
 - Reduce spontaneous MI
 - No significant difference in death