MINOCA Update

Approaches to Diagnostic Testing

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CURRENT OPINION

ESC working group position paper on myocardial infarction with non-obstructive coronary arteries

Stefan Agewall[1]*, John F. Beltrame[2], Harmony R. Reynolds[3], Alexander Niessner[4], Giuseppe Rosano[5,6], Alida L. P. Caforio[7], Raffaele De Caterina[8], Marco Zimarino[8], Marco Roffi[9], Keld Kjeldsen[10], Dan Atar[1], Juan C. Kaski[6], Udo Sechtem[11], and Per Tornvall[12], on behalf of the WG on Cardiovascular Pharmacotherapy

1. Acute Myocardial Infarction (3rd Universal Definition)

- **Cardiac biomarker** – Tn level > 99th percentile + rise and/or fall
- **Clinical marker:** *Ischaemic symptoms* – chest pain or angina equivalent
  Ischaemic ECG – new: ST/T changes, LBBB, pathological Q waves
  Ischaemic Imaging – new: loss of viable myocardium or wall motion

2. Non-obstructive Coronaries on Angiography (<50% lesion)

3. No Clinically Overt Cause for ACS Presentation

Agewall et al (2017) Eur Heart J 38:143-53

AHA SCIENTIFIC STATEMENT

Contemporary Diagnosis and Management of Patients With Myocardial Infarction in the Absence of Obstructive Coronary Artery Disease

A Scientific Statement From the American Heart Association

1. Acute Myocardial Infarction (4th Universal Definition)

- **Cardiac biomarker** – Tn level > 99th percentile + rise and/or fall
- **Corroborative clinical evidence of infarction** (at least 1 of following):
  - *Ischaemic symptoms* – chest pain or angina equivalent
  - *Ischaemic ECG* – new: ST/T changes, LBBB, pathological Q waves
  - *Ischaemic Imaging* – new: loss of viable myocardium or wall motion
  - *Coronary Thrombus* – angiography or autopsy

2. Non-obstructive Coronaries on Angiography (<50% lesion)

- Including – normal, mild lesions (< 30%), moderate (30 to <50%)

3. No Alternate Diagnosis for ACS Presentation

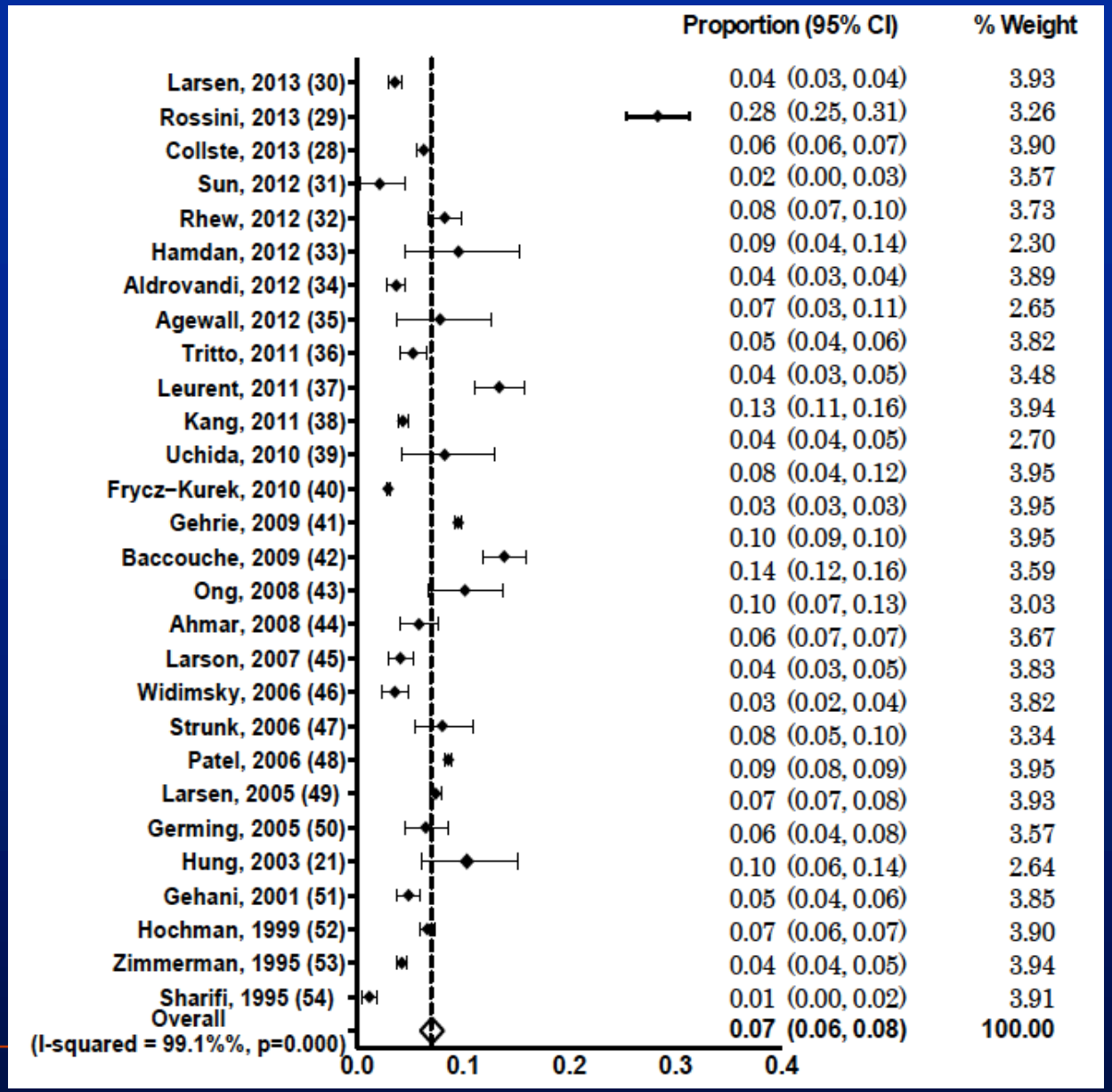
Tamis-Holland et al (2019) Circulation 139:e891-908

MINOCA Prevalence

- Pooled 28 publications
  - AMI + angio findings
  - consecutive recruit
  - at least 100 patients
  - 177,432 AMI patients

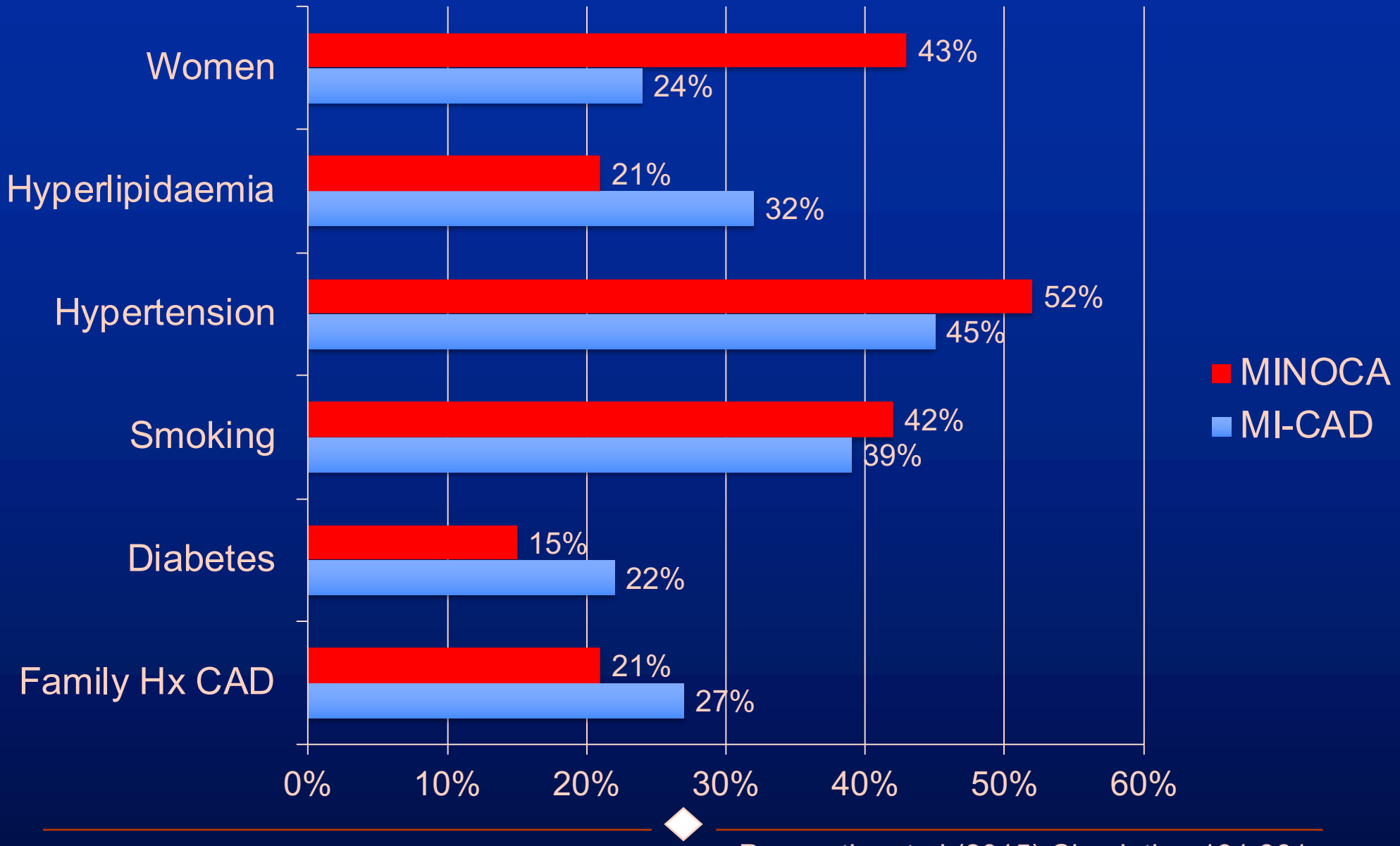
- Overall Prevalence

  7.0% (95%CI: 6%, 8%)



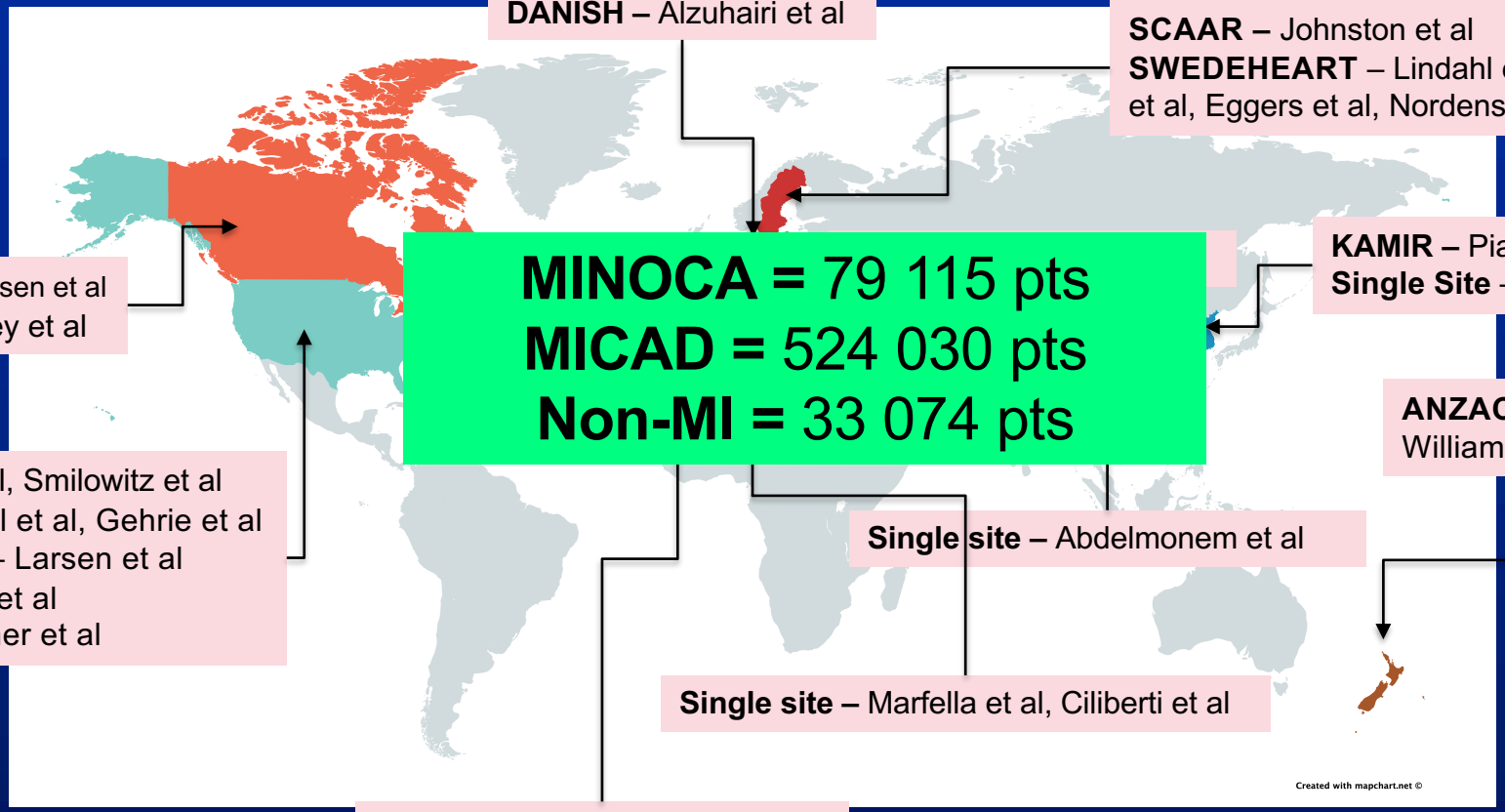
Pasupathy et al (2015) Circulation 131:861

MINOCA Comparative CV Risk Factors



Pasupathy et al (2015) Circulation 131:861

MINOCA Prognosis: Meta-analysis



DANISH – Alzuhairi et al

SCAAR – Johnston et al
SWEDEHEART – Lindahl et al, Baron et al, Eggers et al, Nordenskjold et al

KAMIR – Piao et al, Kang et al
Single Site – Rhew et al

ANZACS-QI - Barr et al, Williams et al

APPROACH – Larsen et al
ALBERTA – Bainey et al

MINOCA = 79 115 pts
MICAD = 524 030 pts
Non-MI = 33 074 pts

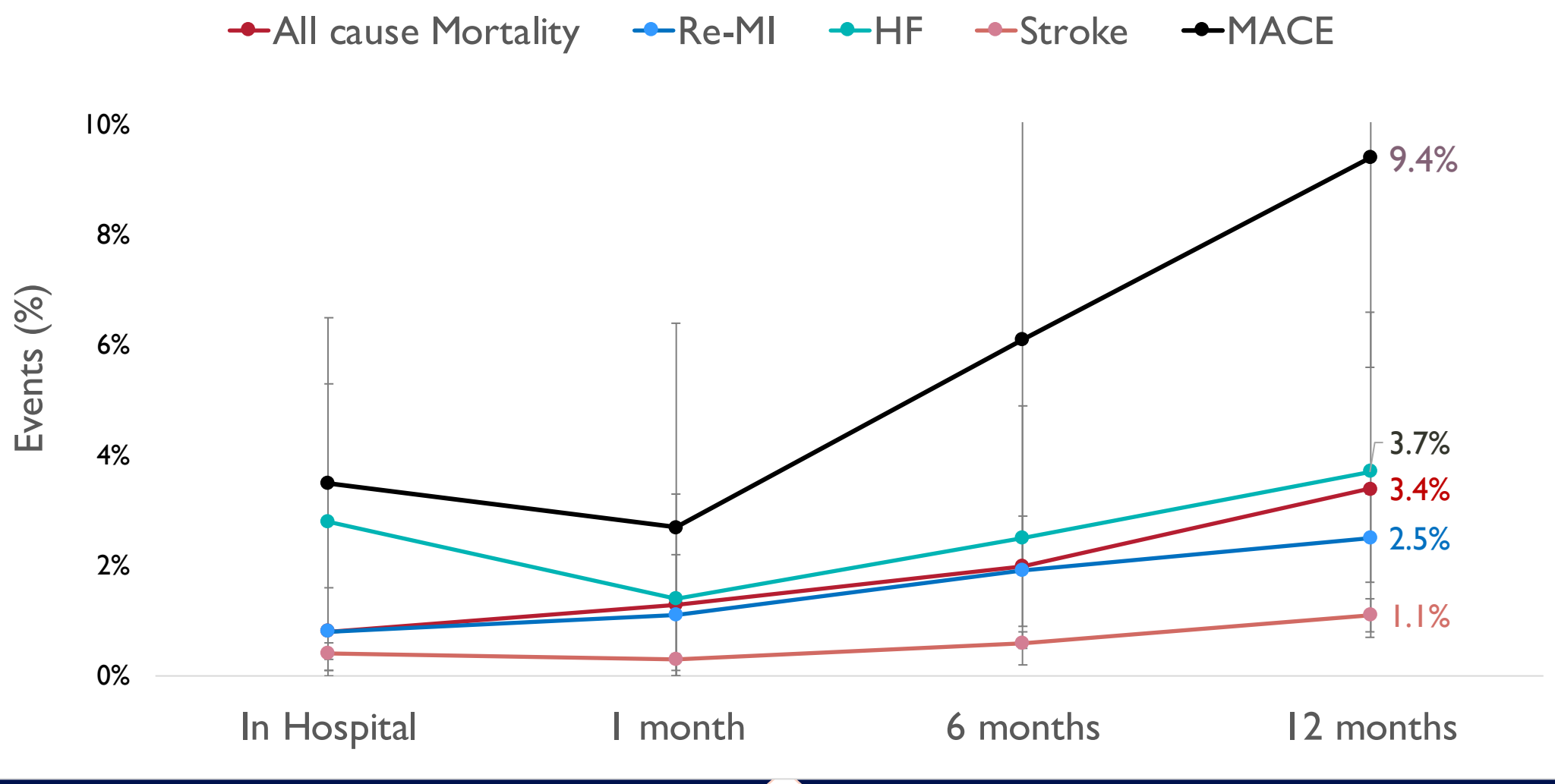
NCDR – Najib et al, Smilowitz et al
CRUSADE – Patel et al, Gehrie et al
HORIZONS-AMI – Larsen et al
ACUITY – Planer et al
Single Site – Turner et al

Single site – Abdelmonem et al

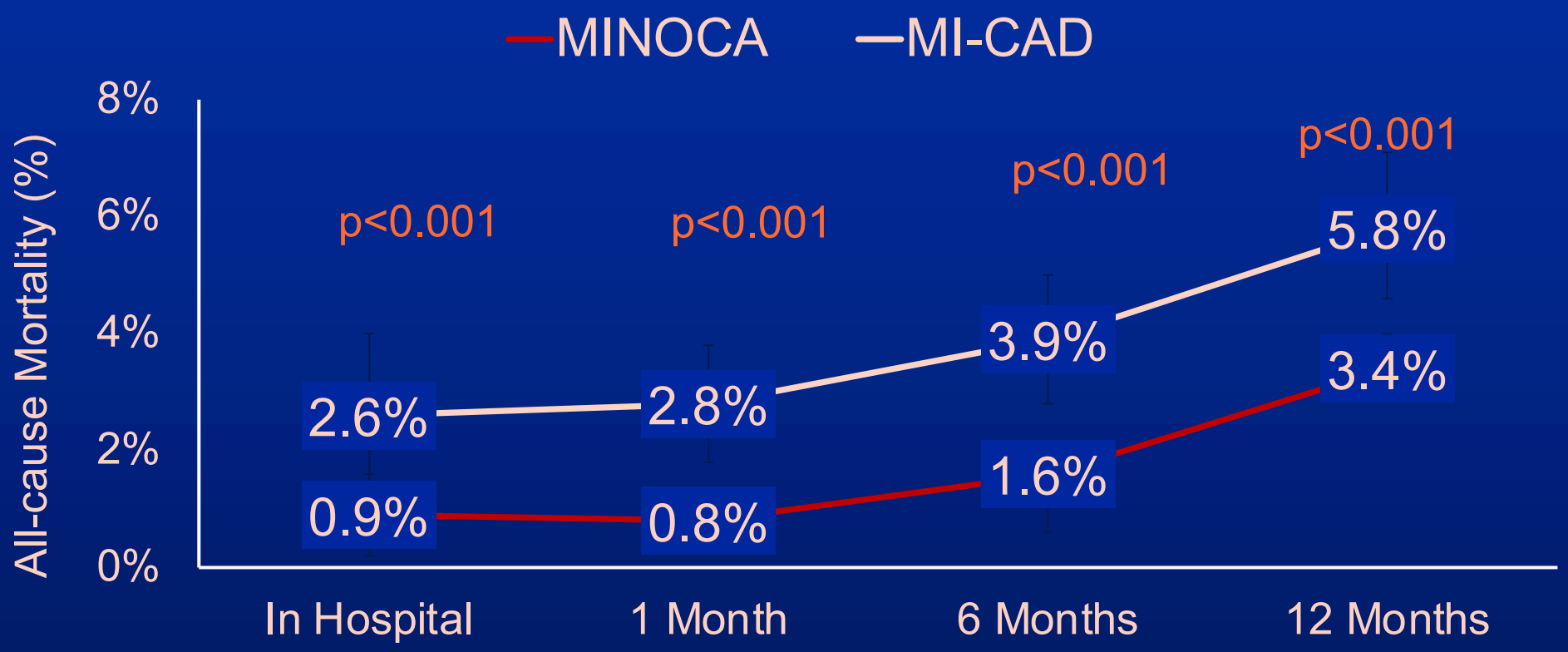
Single site – Marfella et al, Ciliberti et al

Single site – Montenegro et al

MINOCA Prognosis: MACE

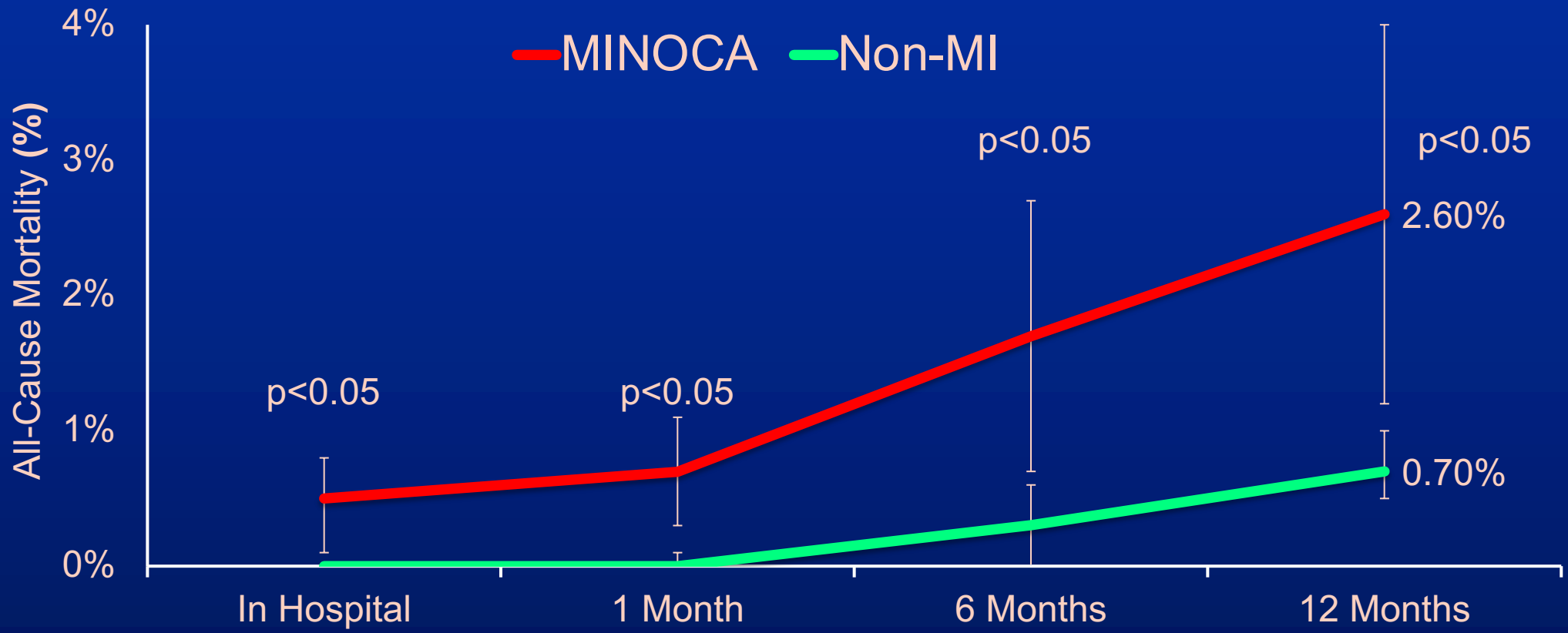


MINOCA Vs MI-CAD: All Cause Mortality



MINOCA (n)	37191	16789	15692	16642
MI-CAD (n)	500520	179766	163684	174461

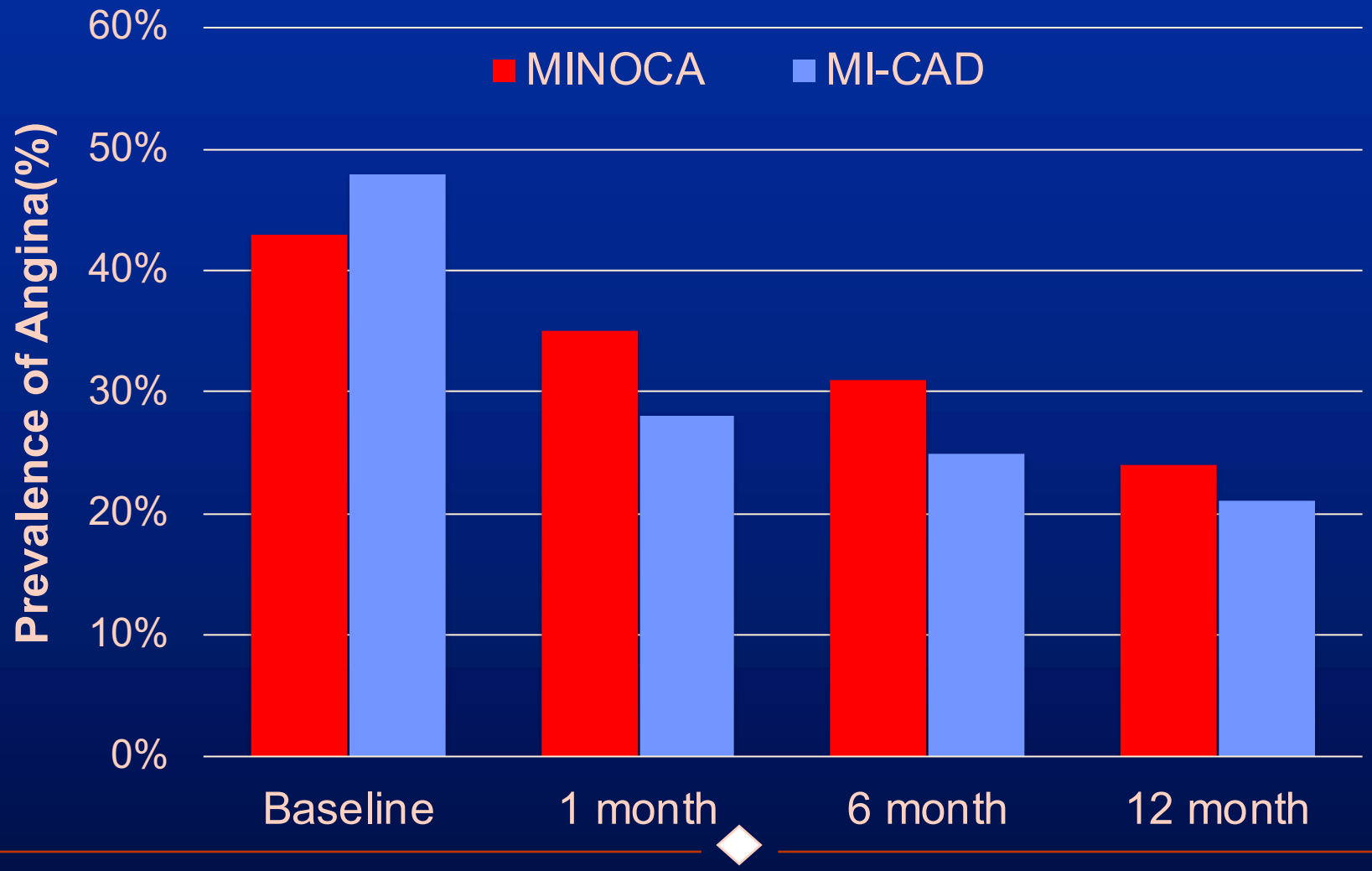
MINOCA Vs Non-MI: All Cause Mortality



MINOCA (n)	8465	8465	8465	8465
Non-MI (n)	33074	33074	33074	33074

MINOCA Comparative Symptom Status

Post-infarct angina occurs in 1/4 MINOCA patients in the following 12 months



Grodzinsky et al (2015) EHJ QCCO 1:92-9

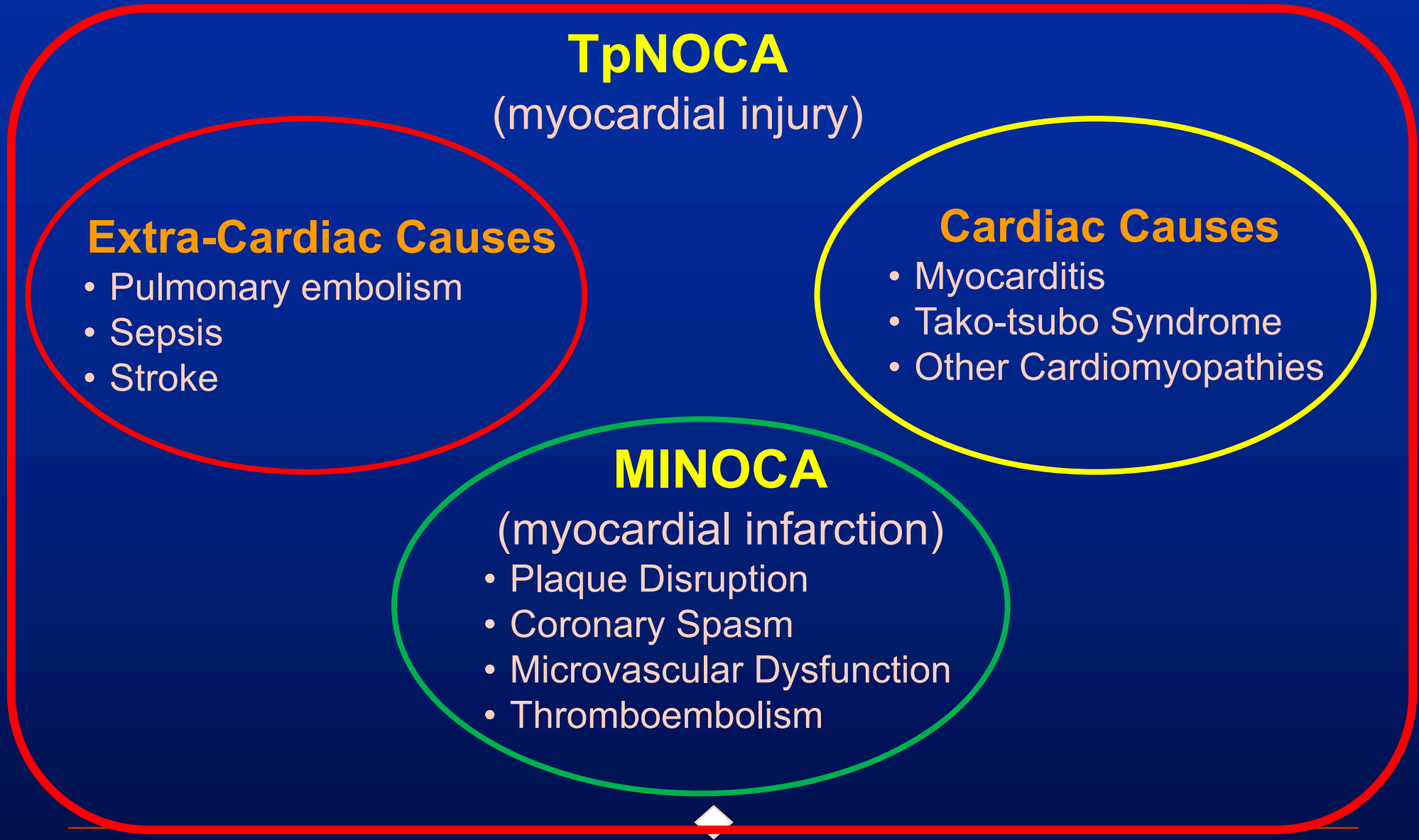
Challenges in defining MINOCA

- MINOCA as a specific term
  - Ischaemic necrosis / true myocardial infarct

- MINOCA as a *generic term* *(myocardial injury)*
  - Alternative term – TpNOCA
    (Troponin positive with Non-Obstructive Coronary Arteries)

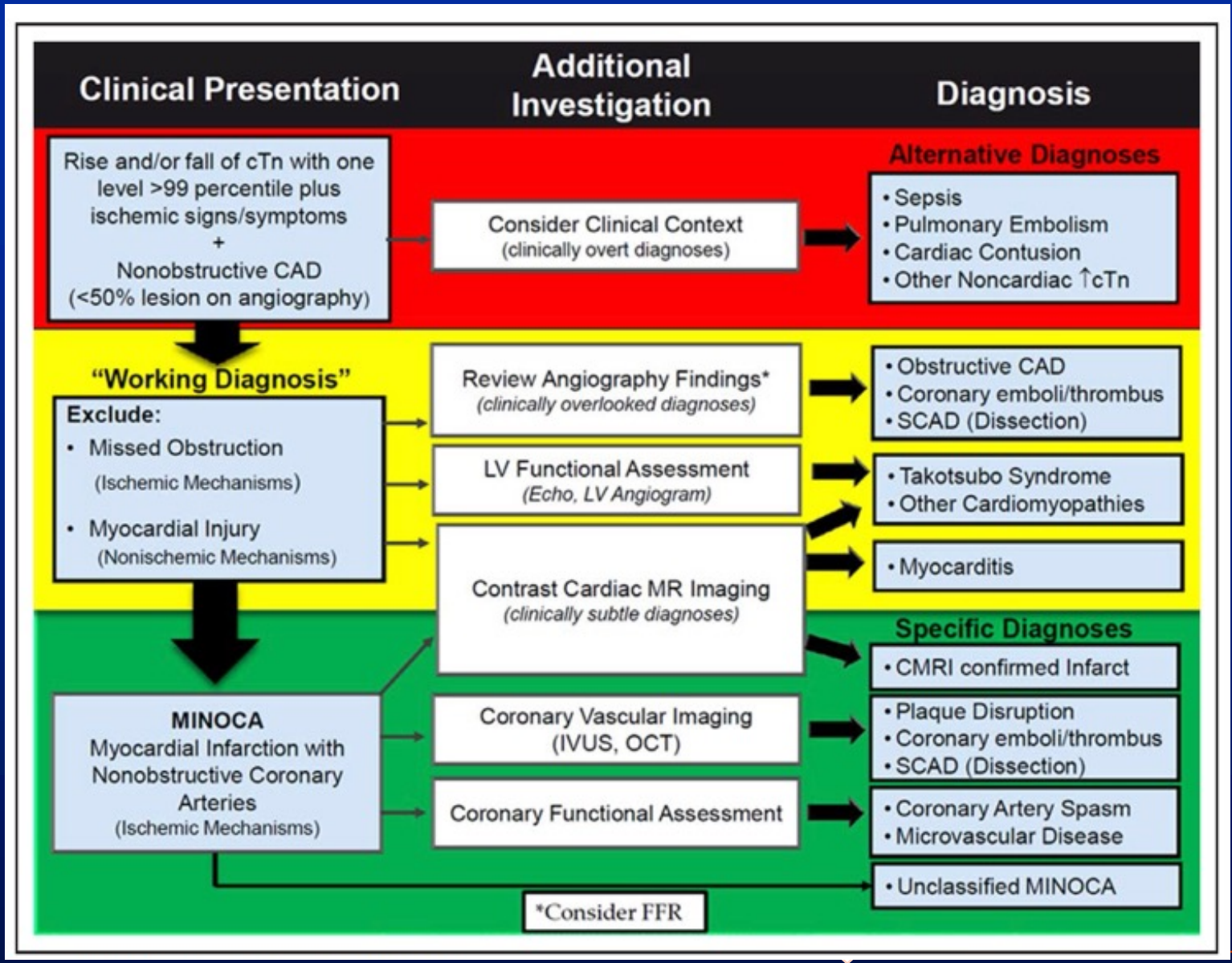
Adapted from Pasupathy et al (2017) Circulation 135:1490-3

Troponin Positive Non-Obstructive Coronary Arteries



Adapted from Pasupathy et al (2017) Circ 135:1490-3

The 'Traffic Light Approach' for TpNOCA & MINOCA



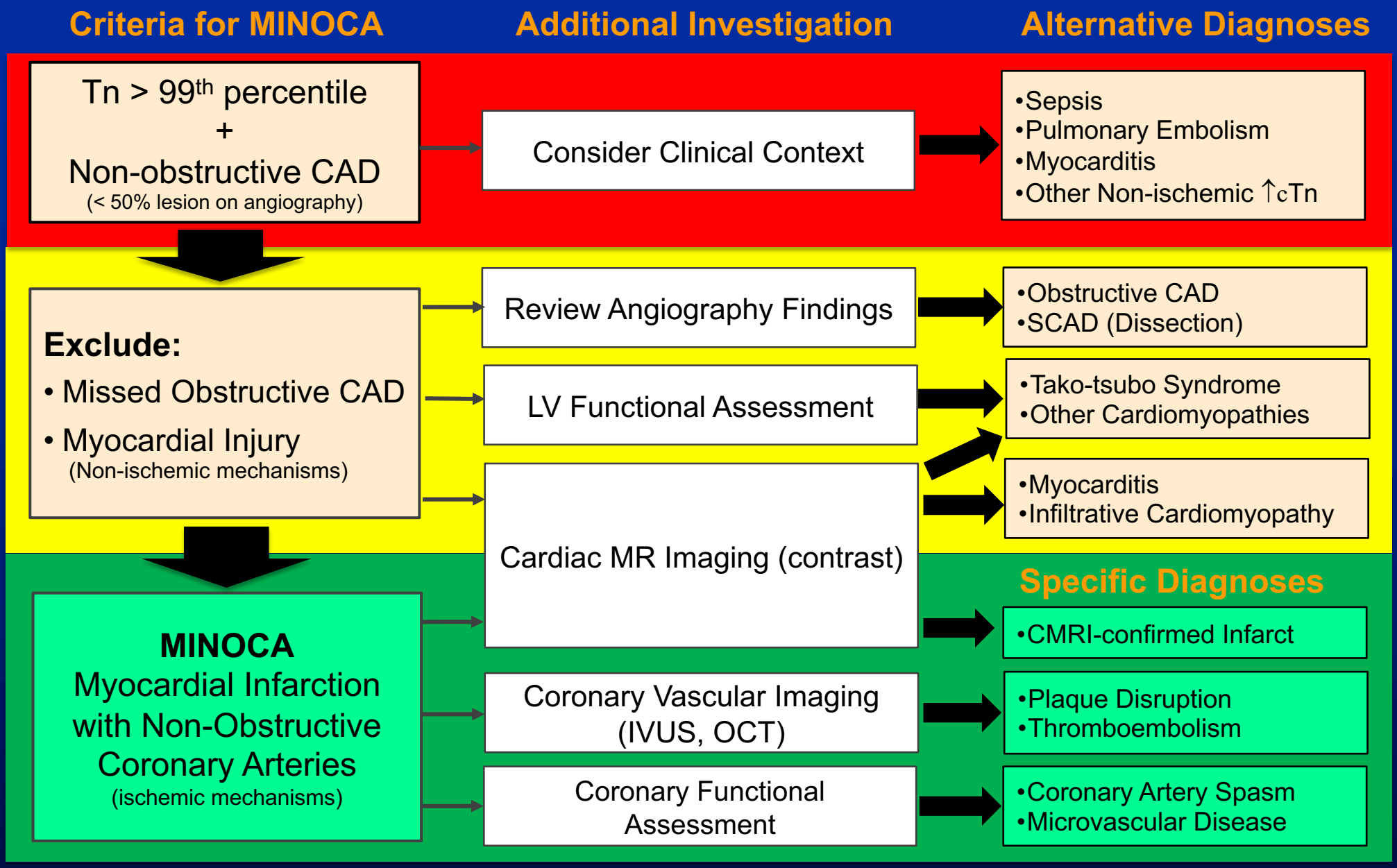
TpNOCA
(myocardial Injury)

Working Diagnosis

MINOCA
(myocardial Infarct)

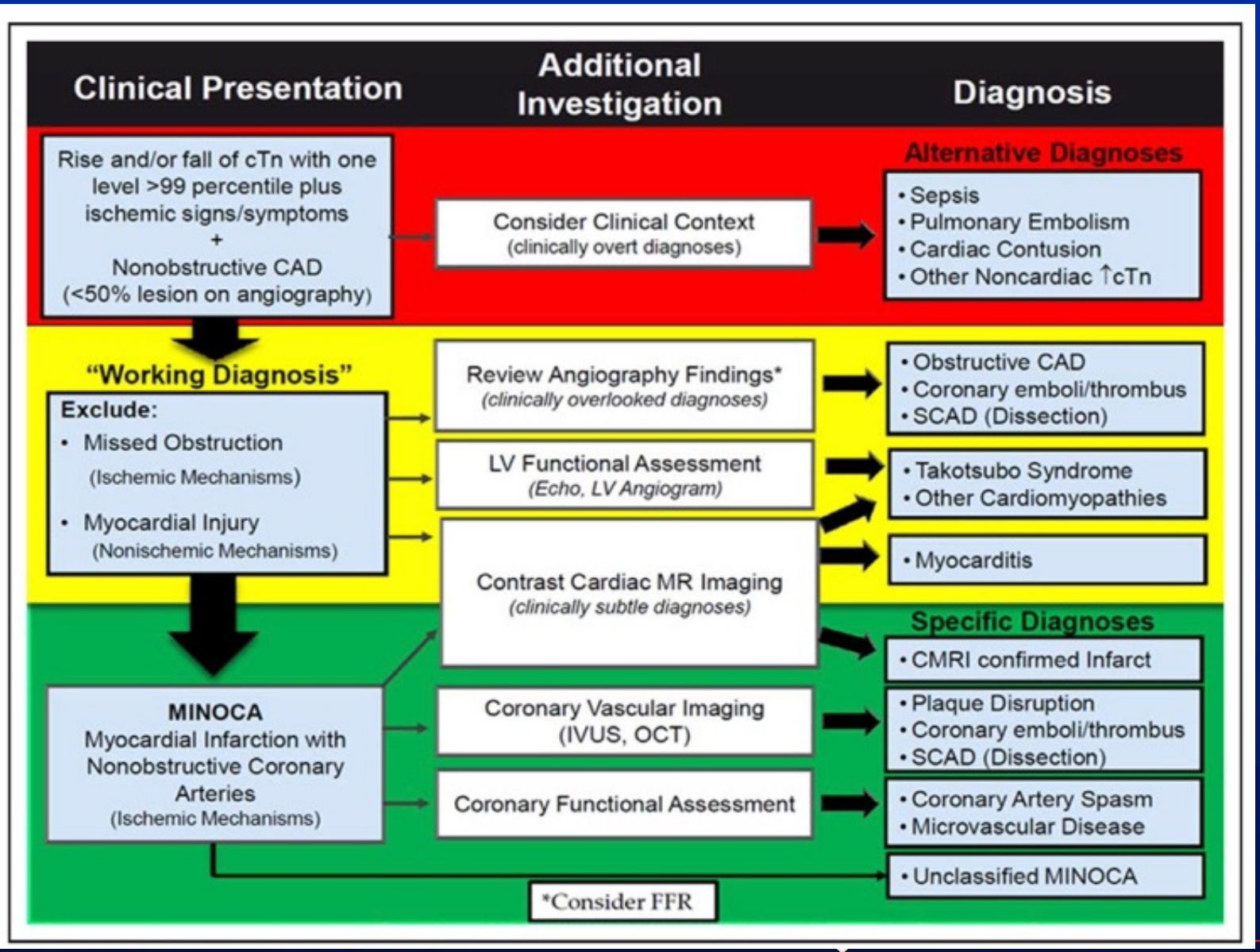
Tamis-Holland et al (2019) Circulation 139:e891-908

The 'Traffic Light Approach' for TpNOCA & MINOCA



Tamis-Holland et al (2019) Circulation 139:e891-908

Identifying the Causes for 'MINOCA' – how far?



MINOCA Diagnosis
- History
- Serial Troponin
- ECG

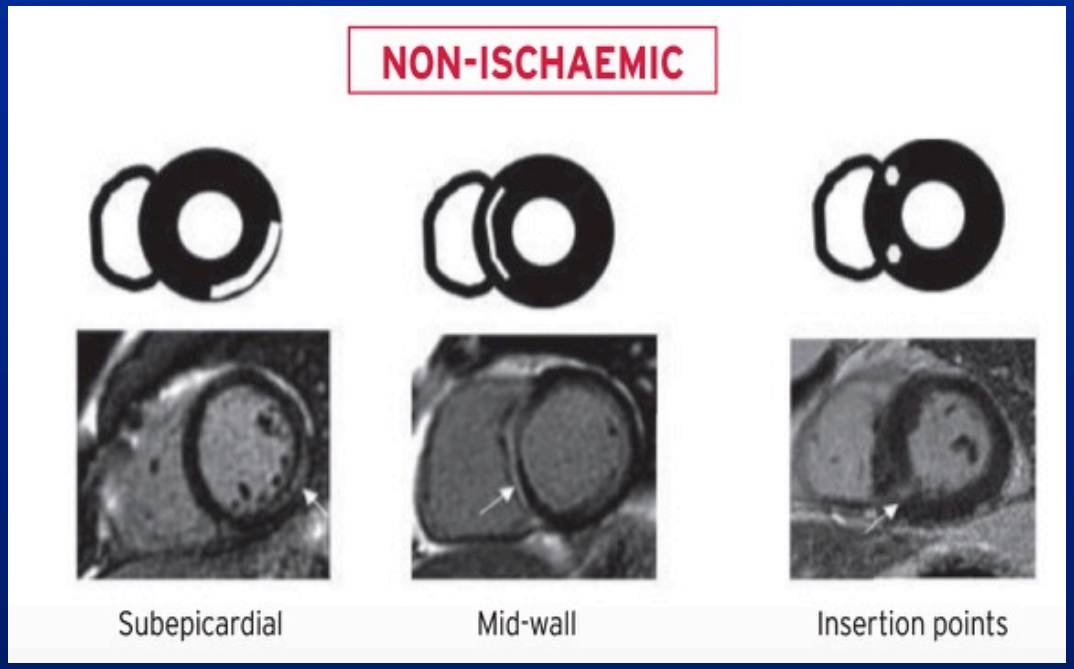
- Review Angio
- LV Assessment
- Cardiac MRI

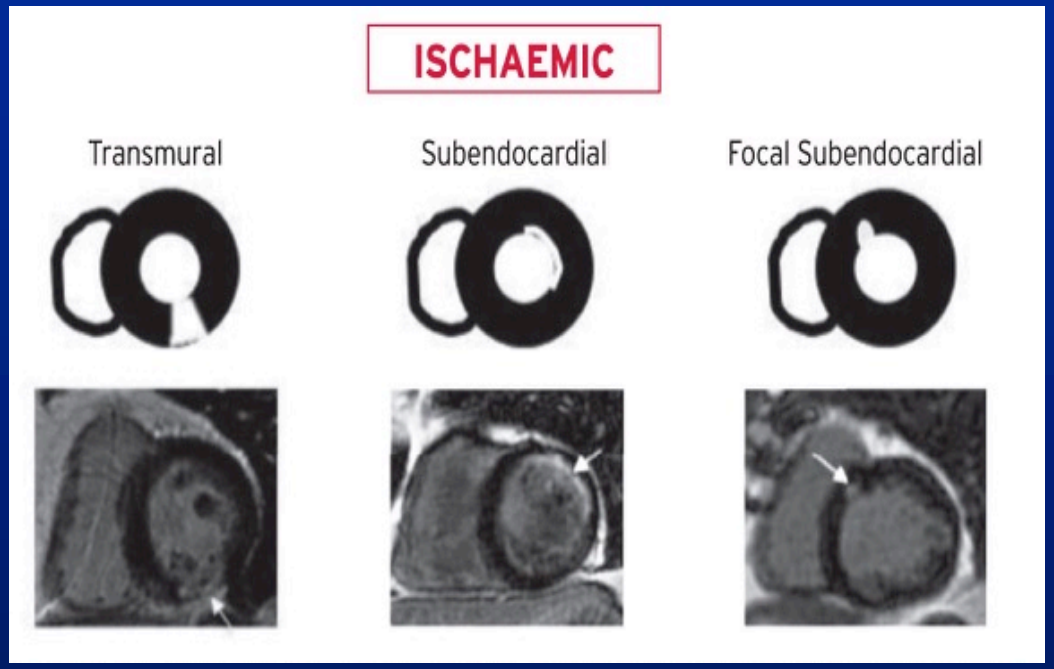
MINOCA Causes
- IVUS
- OCT
- ACh Spasm
- iMR / hMR
- Thrombophilia

Tamis-Holland et al (2019) Circulation 139:e891-908

Utility of Cardiac MRI in MINOCA

- Demonstration of myocardial injury (oedema/inflammation)
- Confirmation of myocardial infarction (fibrosis)



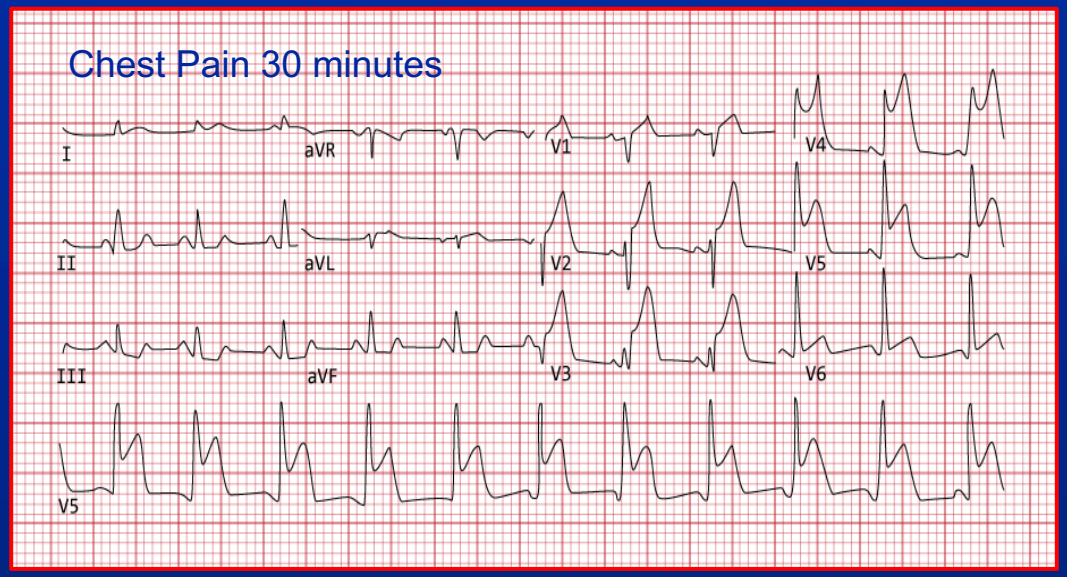


Consistent with myocarditis

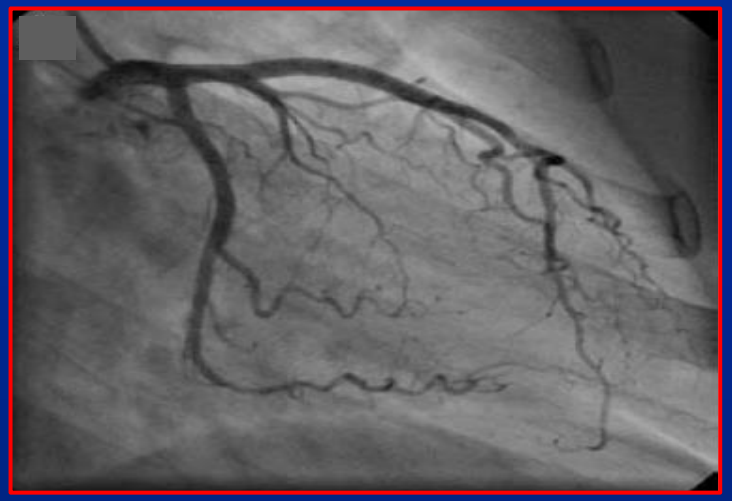
Consistent with myocardial infarction

Thygesen et al (2019) Eur Heart J 40:237-69

Pathophysiology - MINOCA



↑Serial Troponin T



Potential Myocardial Infarct Mechanisms

Type 1 MI

Plaque Disruption

Plaque Erosion, Rupture

Type-2 MI

↓Myocardial Perfusion

Coronary Spasm, Embolism, MV Dysfunction

↑Myocardial Oxygen Demand

Sustained Tachyarrhythmia, LVH / Hypertensive

Plaque Disruption in MINOCA

Plaque Rupture Benchmark Vascular Imaging Studies:

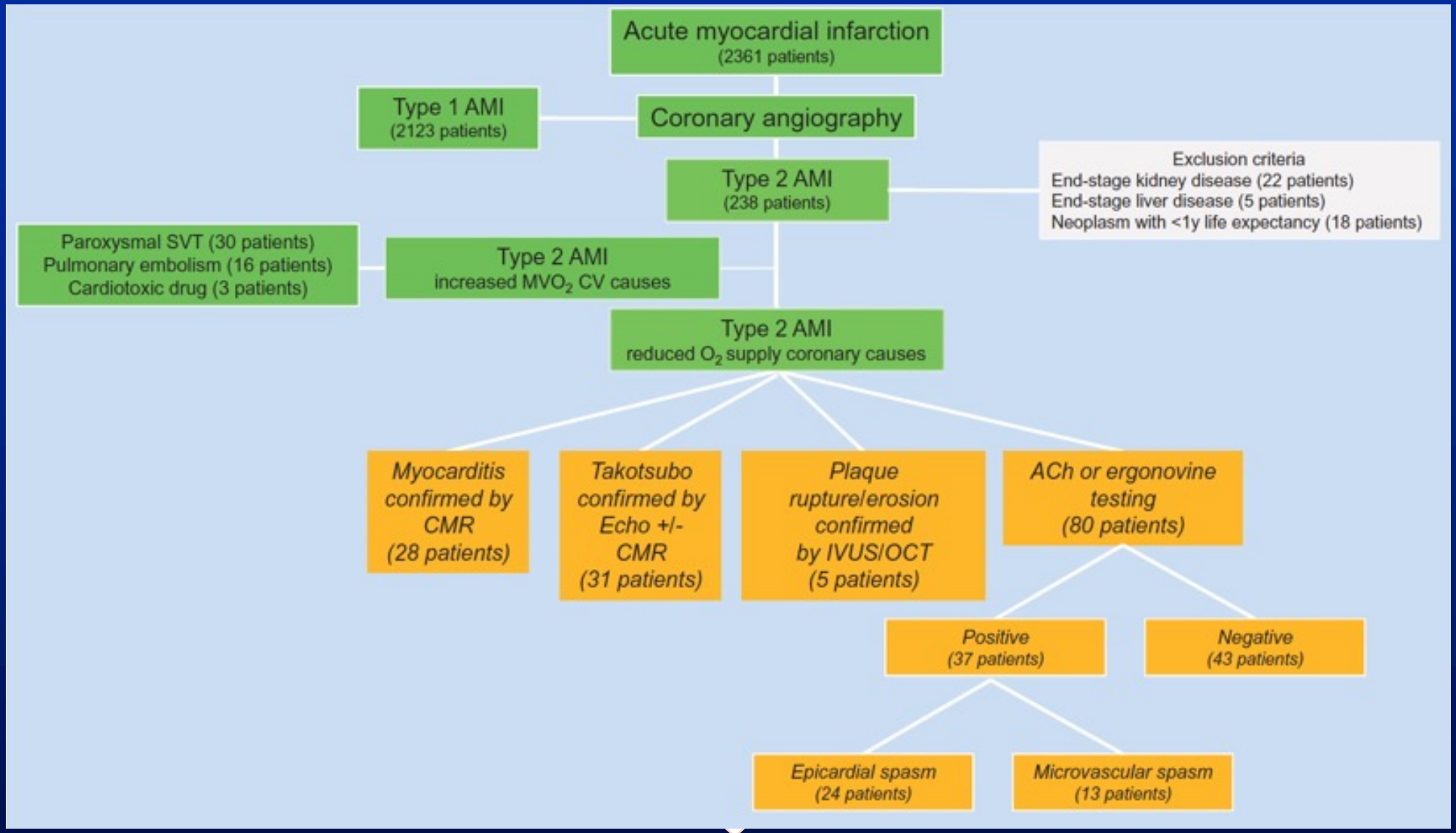
- Stable CAD (IVUS ~1 year postSTEMI) → 4% (HORIZONS-AMI)
- STEMI (OCT ~2 hours) → 49% (OCTAVIA)

MINOCA cohort studies

- MINOCA (IVUS ~2 days) 50 women → **38%**
- MINOCA (IVUS, <24 hrs) 68 men & women, → **37%**
- No angiographically normal pts had plaque disruption (small studies)

Reynolds et al Circ 2011, Ouldzein H et al Ann Cardiol Angeiol 2012, Guagliumi et al JACC Interventions 2014, Souza et al Cor Art Dis 2015

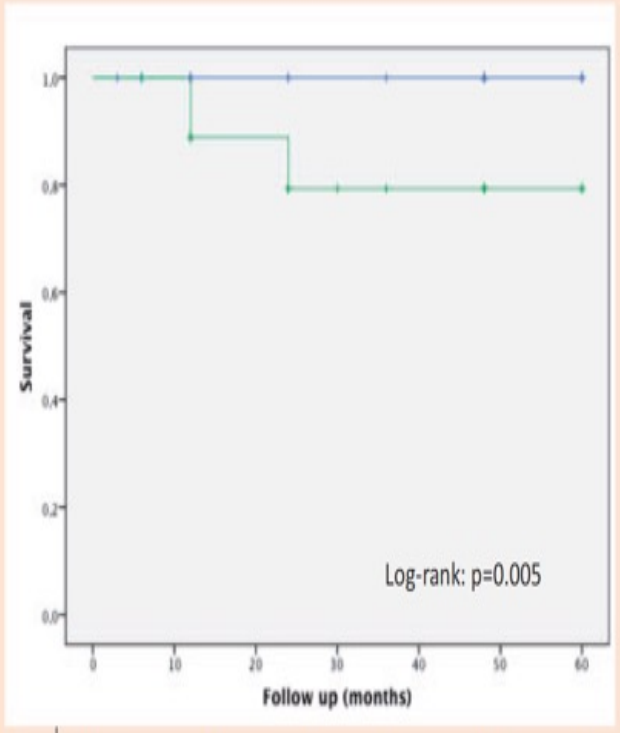
MINOCA: Spasm Testing



Montone et al (2018) EHJ 39:91-8

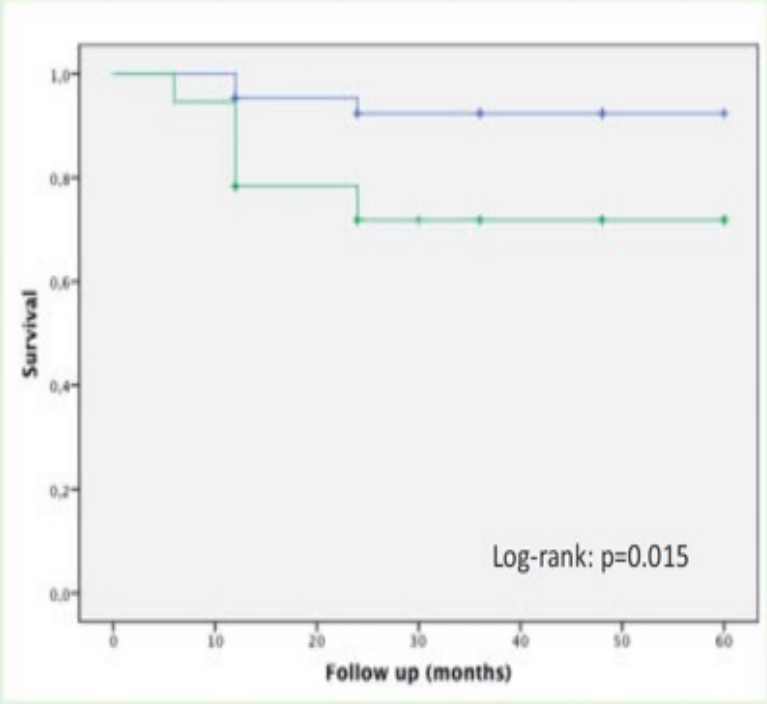
MINOCA: Spasm Testing Outcomes

Cardiac Death



No. at risk	0y	1y	2y	3y	4y	5y
Positive test	37	34	27	15	11	7
Negative test	43	42	33	23	14	3

ACS Readmissions



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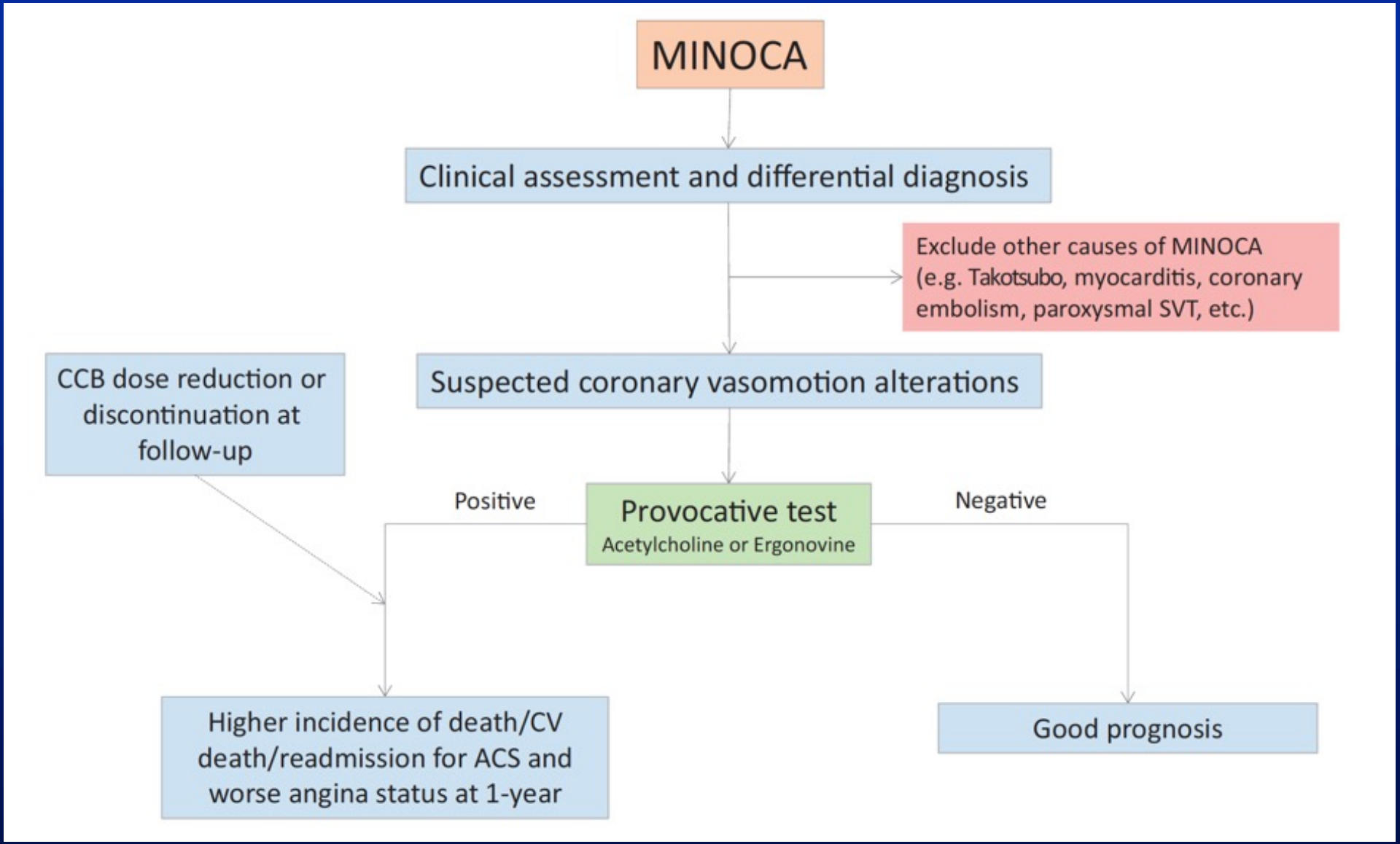

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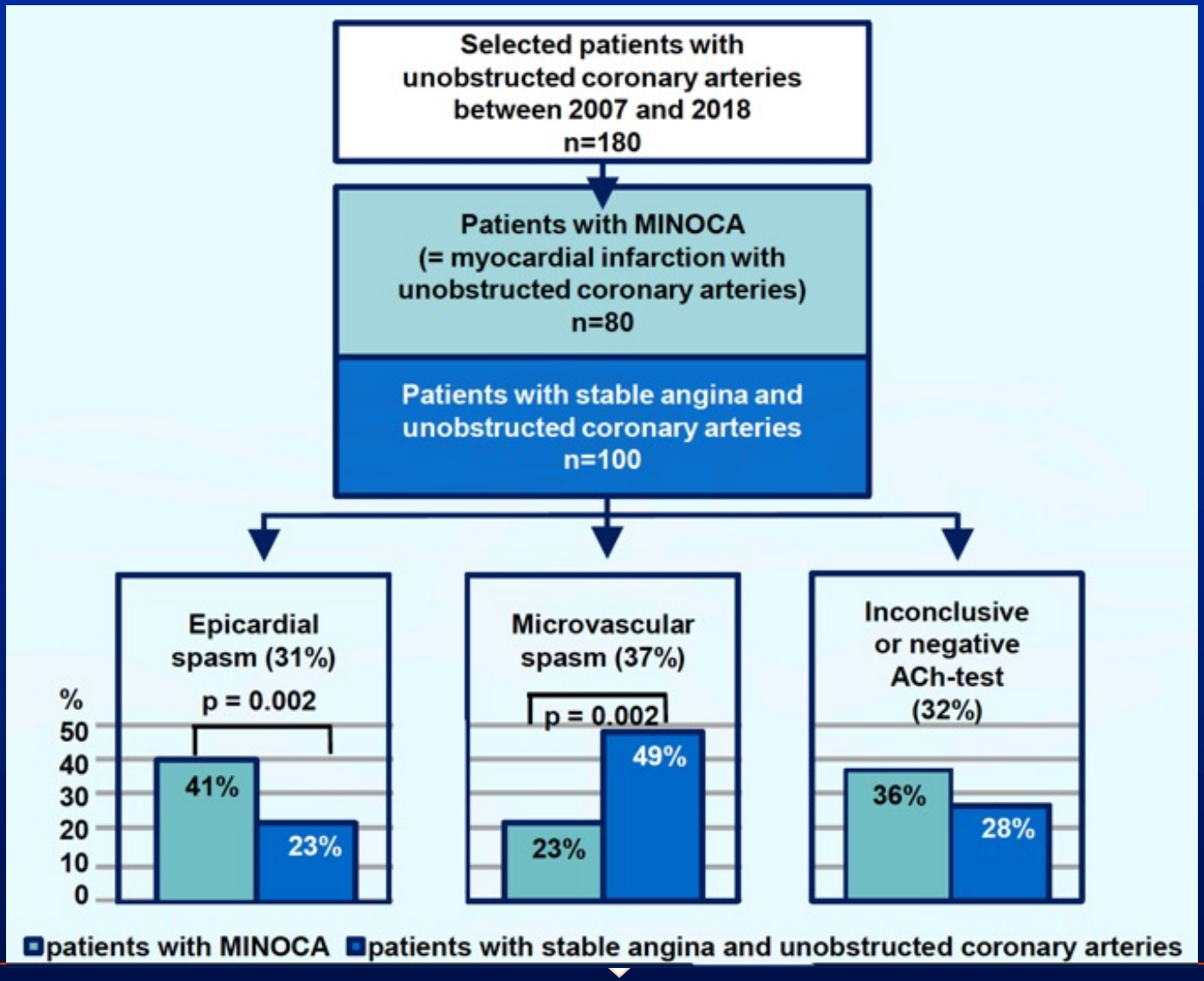


Probst et al (2019) ESC Congress

Why Diagnose 'MINOCA'?

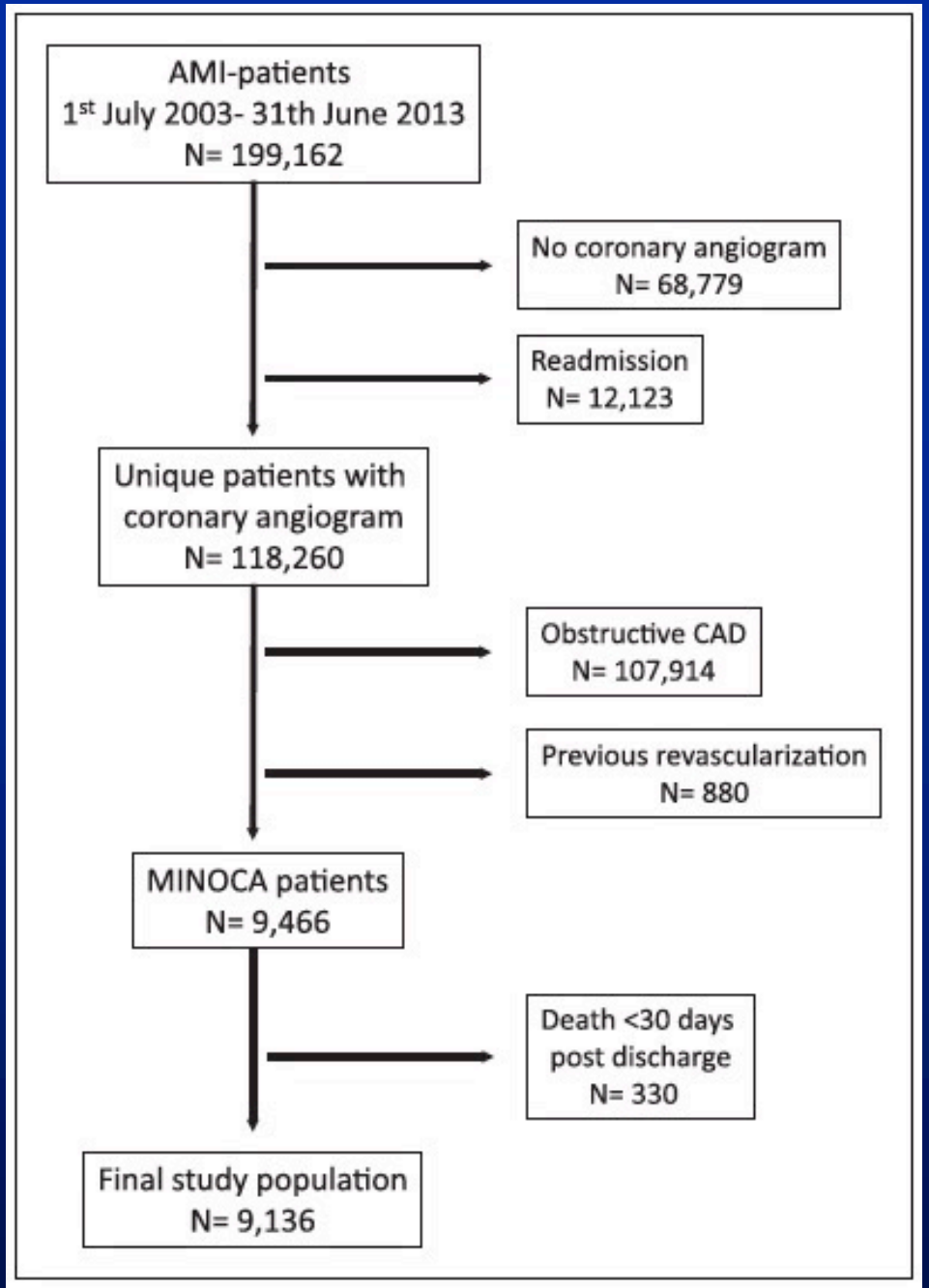
- Clinical Recognition
  - 'False positive STEMI Diagnosis'
- Clinically differs to Obstructive CAD
  - Clinical Profile – over-represented in women & young
  - Prognosis – better than MICAD but worse than No-MI
  - Mechanisms – spasm, emboli, microvascular dysfunction
  - Therapies – calcium channel blockers, anti-thrombotics
- Evaluation of Underlying Cause
  - Extra-cardiac - pulmonary emboli, stroke, sepsis
  - Cardiac – Ischaemic vs Non-ischaemic Causes

MINOCA: Challenges for COVADIS

- Routine Cardiac MRI
- Routine Spasm Testing in MINOCA?
  - Which patients?
  - When test?
- Role of IVUS / OCT?
- Therapy?

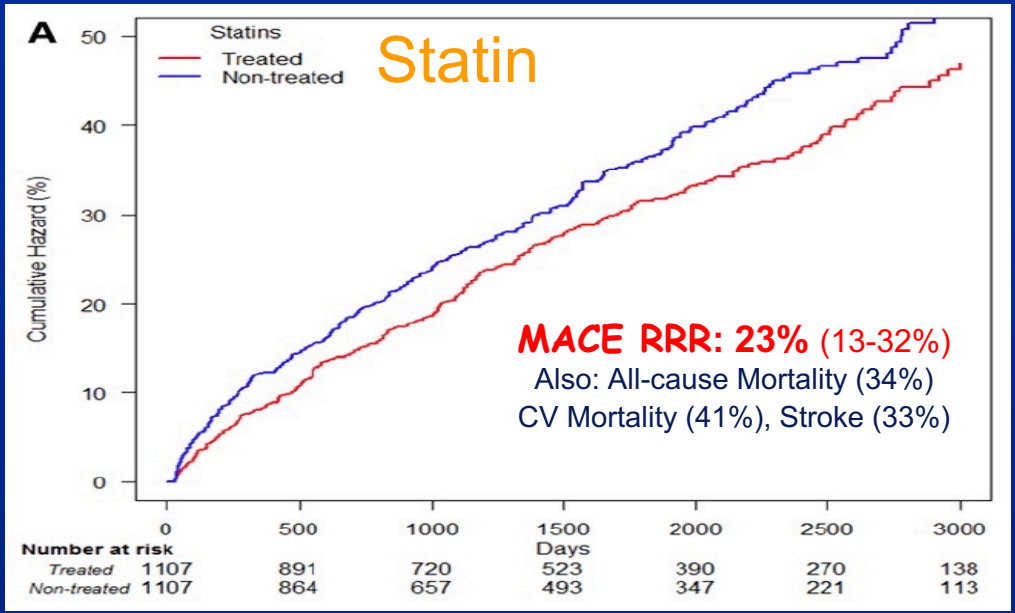
SWEDEHEART Study

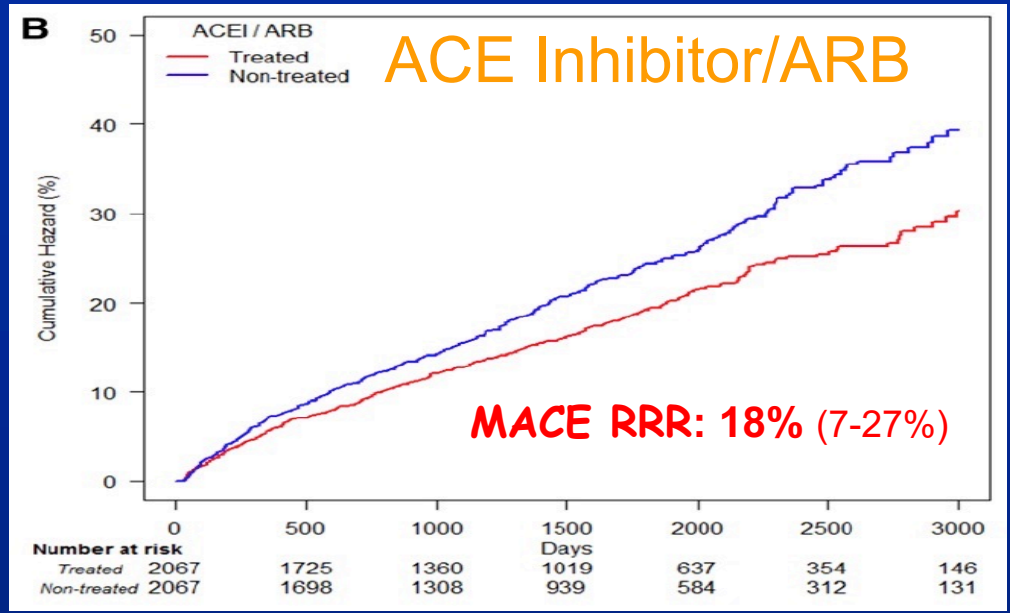
- Consecutive AMI pts 2003-2013
- MINOCA: AMI Discharge Dx
  Angio <50% stenosis
- Primary Endpoint: MACE
  - all-cause mortality
  - Hospitalization (MI, stroke, heart failure)
- Follow-up: 4.1 years (30d – 2013)
- Stratified propensity analysis
  - Dual Anti-platelet Agents
  - Statins
  - ACE-Inhibitors /Ag Receptor BI
  - Beta Blockers

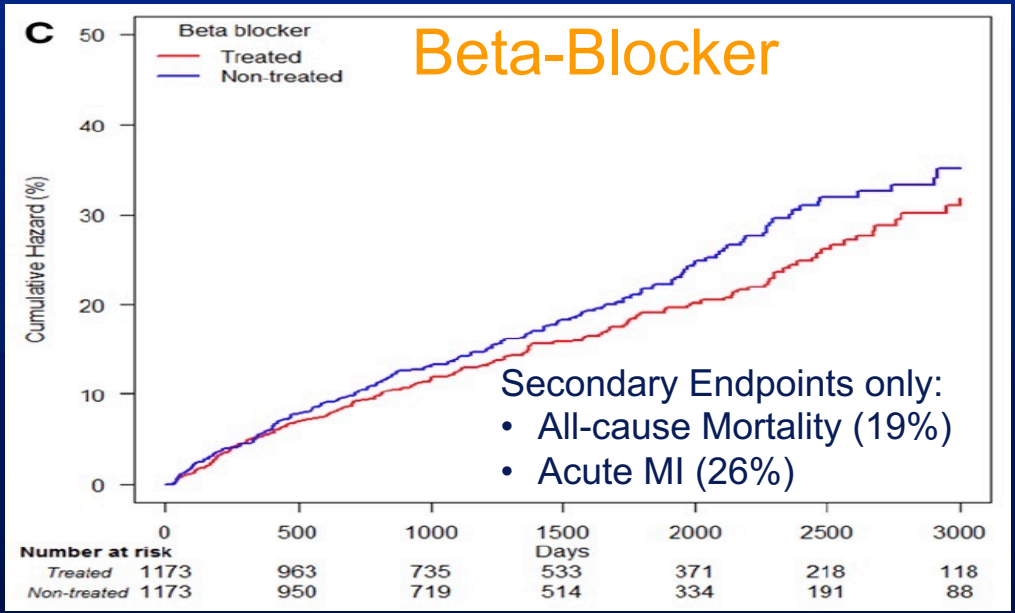


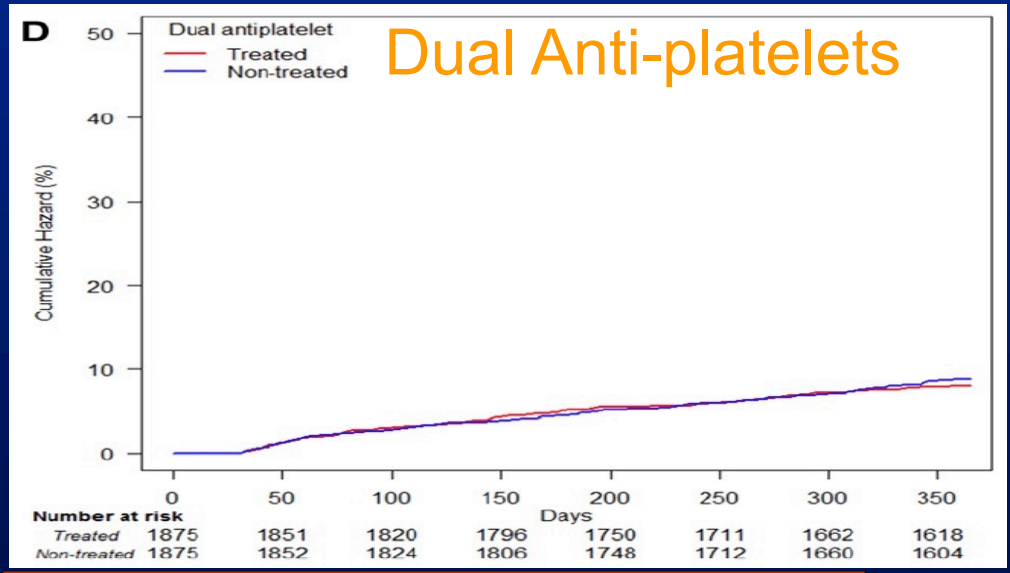
Lindahl et al (2017) Circ 135:1481-9

SWEDEHEART: MINOCA









Lindahl et al (2017) Circ 135:1481-9

MINOCA-BAT Study

Acute MI + Non-obstructed Coronaries

- β-Blocker⊖ ACE-I/ARB⊖
- β-Blocker⊕ ACE-I/ARB⊖
- β-Blocker⊖ ACE-I/ARB⊕
- β-Blocker⊕ ACE-I/ARB⊕

6 week Review: clinical review & medication check

4-year Outcomes: all-cause death, recurrent heart attack, stroke, or heart failure

(Recruit = 3,500 MINOCA patients)