Diuretica bij hartfalen

waarom, hoeveel en hoe?

Practopics Plus
28 mei 2021
dr. Philippe Mortelmans
cardiologie GZA

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Inhoud

1. examen
2. algemene concepten
3. soorten diuretica
4. dosering
5. nierinsufficiëntie
6. diureticaresistentie
7. ambulante opvolging
8. animal farm
9. 10 sleutelprincipes

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1. Ten opzichte van betablokkade en ACE-inhibitie is de prognostische waarde van diuretica bij HF…

a. kleiner
b. even groot
c. groter
d. wie weet dat?

2. Bij een stijging van het serumcreatinine zal ik de diureticumdosis gewoonlijk…

a. verhogen
b. onveranderd laten
c. verlagen
d. laten afhangen van KOZ

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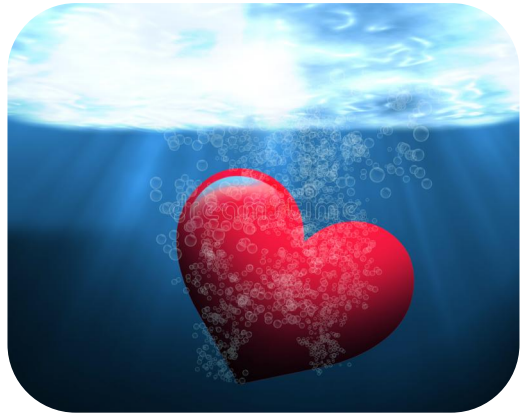

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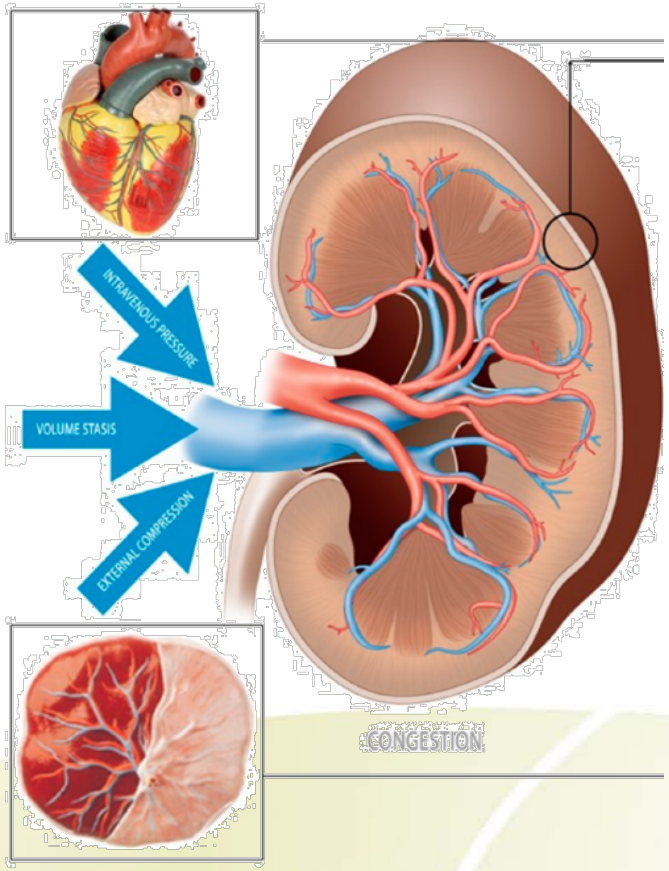
4. Wat is het meest frequente mechanisme achter nierfunctie-achteruitgang bij hartfalen?

a. gedaalde cardiac output
b. veneuze congestie



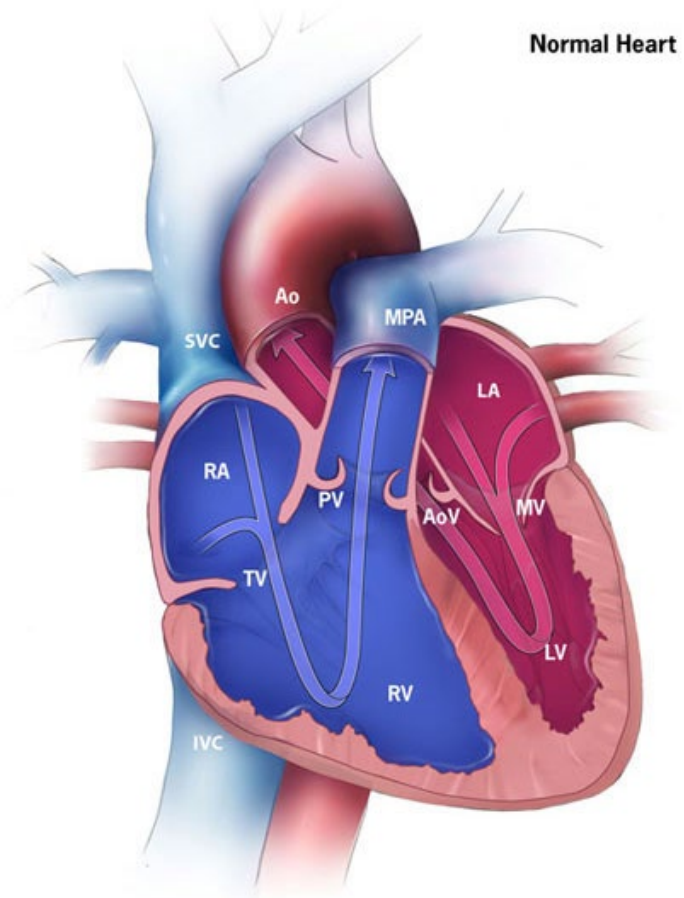
Doel?

"The aim of diuretic therapy is to achieve and maintain euvolaemia" guidelines hartfalen 2016

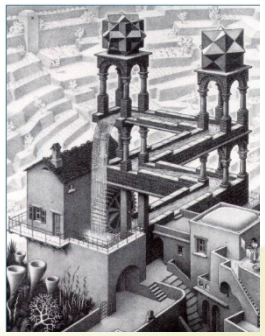
"At the moment no reliable practical bedside test exists to determine euvolaemia"

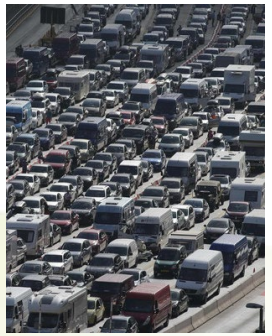
Mullens et al. Eur J Heart Fail 2019

basisprincipes



- bloed stroomt alleen van hoge naar lage druk
- op plaats van probleem vermindert de doorgang
- stroomopwaarts zal (moet) de druk stijgen
- druk in de longen geeft dyspnee





overvulling vs congestie

te veel water

diuretica

(+ hartfalentherapie)

re = v cava inf
li = diastolische functie

hartfalentherapie

1. Ten opzichte van betablokkade en ACE-inhibitie is de prognostische waarde van diuretica bij HF…

a. kleiner
b. even groot
c. groter
d. wie weet dat?

- individualiseren
- laagst mogelijke dosis
- bij hypotensie: liever diureticum verminderen dan ACE-I / BB

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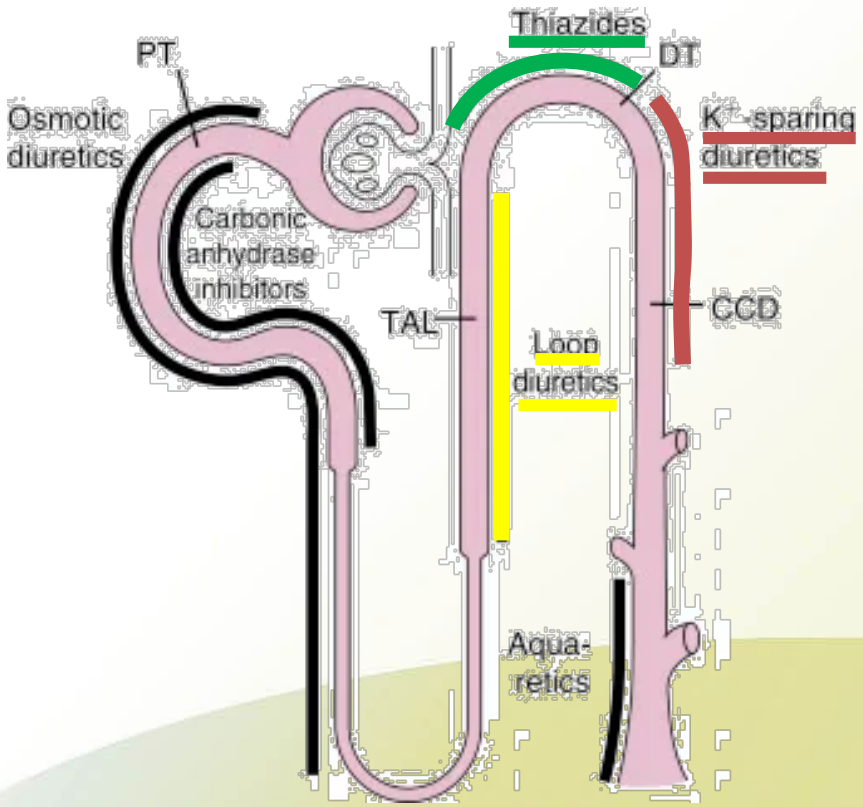
nefron



	bumetanide *Burinex®*	furosemide *Lasix®*	thiazide	spironolactone *Aldactone®*
plaats	TAL	x3	vroege DT	late DT
biol. besch. (%)	80-100	10-100	65-95	90
FENa%	20-25		5-8	2
max dosis (mg)	10-15	400-600		50-100
	1mg bumetanide = 40mg furosemide			

gebruik Burinex ®
(of Torrem®)

Ellison et al. NEJM 2017

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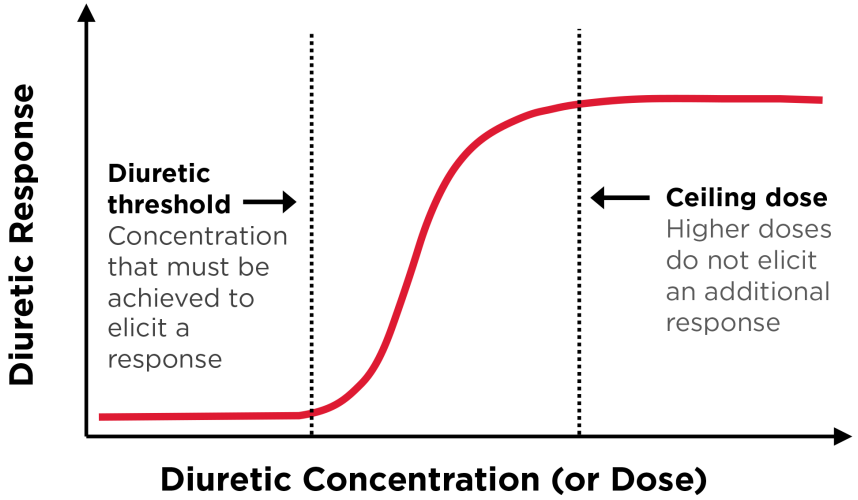
dosering



Adapted from:
Cardiology. 2001;96(3–4):132–43.

ATRIUM CARDIOLOGY COLLABORATIVE

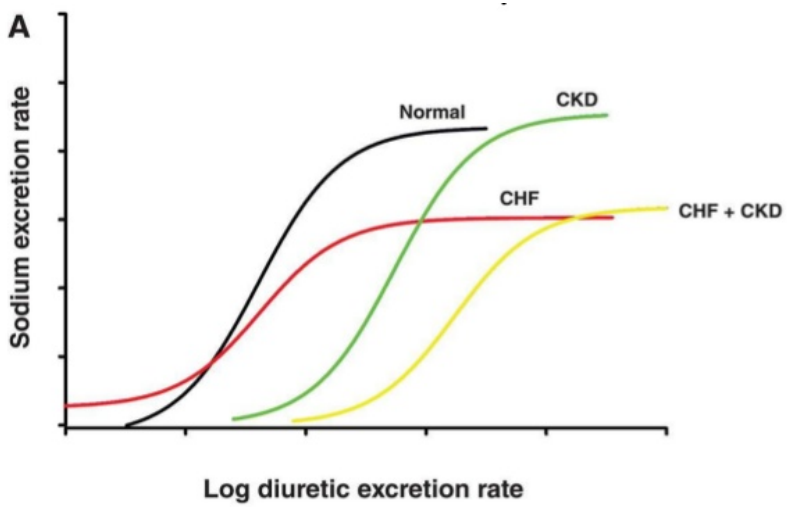


Fig: Dose–response curves for diuretics in normal subjects, patients with chronic kidney disease (CKD), chronic heart failure (CHF) and both renal disease and heart failure.

Voldoende hoge dosis, zeker bij CKD en HF

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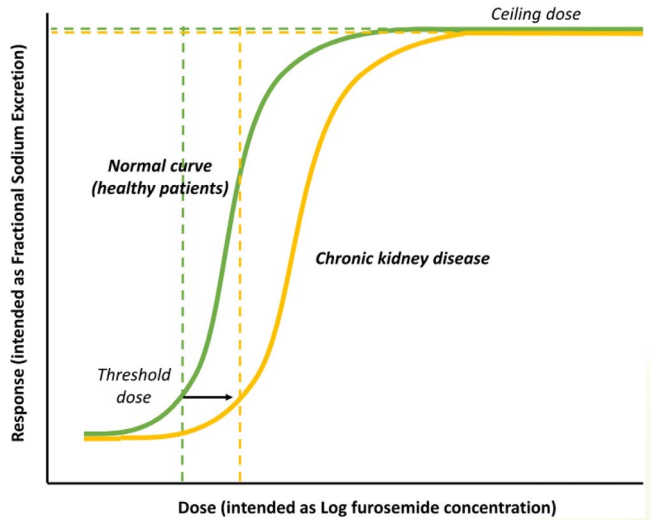
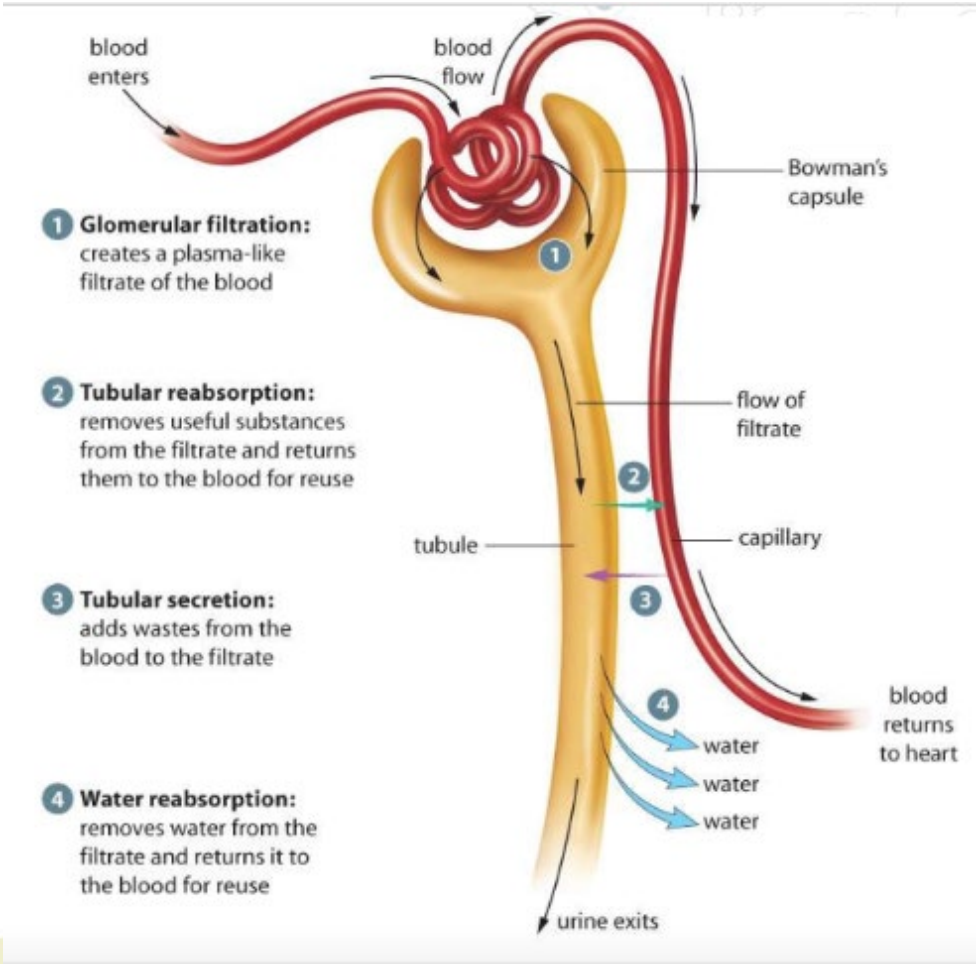
nierinsufficiëntie

- diureticum werkt in het lumen
  - secretie >> filtratie
- enkel gefilterd Na^+ is beschikbaar

nierinsufficiëntie

=> **hogere** dosis nodig voor zelfde effect





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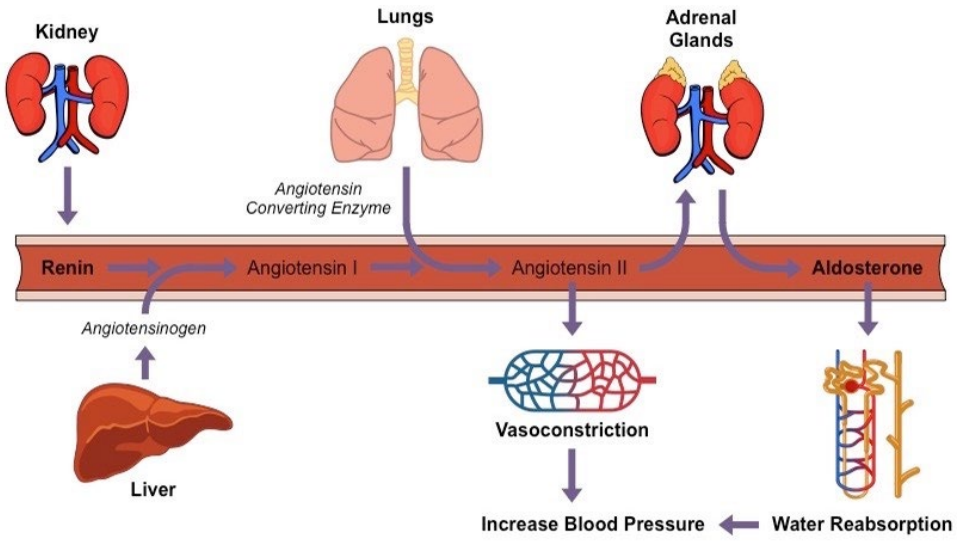
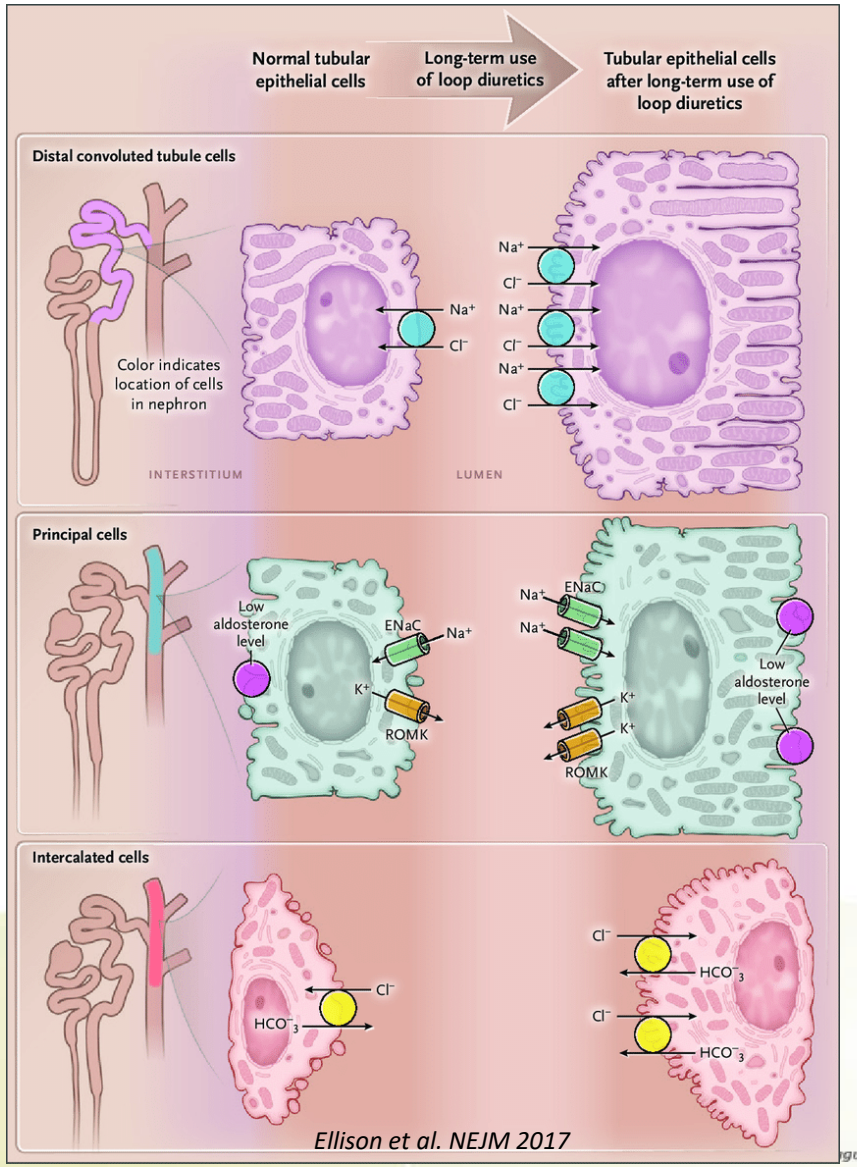
diureticaresistentie

= fysiologische adaptaties waardoor diuretisch effect afneemt

mechanismen

- RAAS↑
  - ←relatieve hypovolemie
  - ← lisdiuretica
- nefronhypertrofie:
  distale Na^+-reabsoprtie ↑





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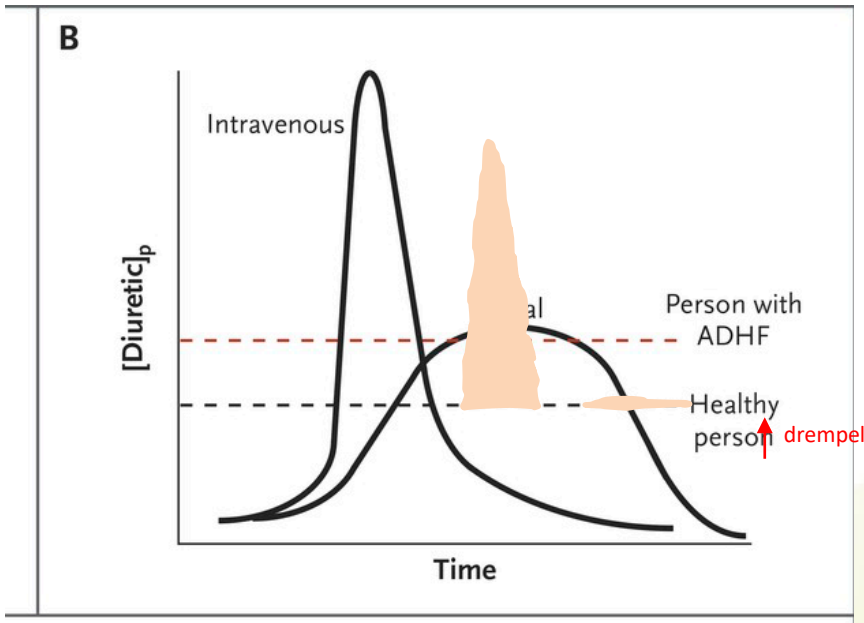
diureticaresistentie: versterkende factoren

- congestie: intestinaal oedeem
  --> absorptie diureticum ↓
- neurohormonale activitatie
- te hoge intake
- NSAID
- nefrotisch syndroom

- intraveneus
  - hogere piek + langer boven drempel
- hartfalenbehandeling
- vocht- en zoutbeperking
- vermijden
- nefroloog



Ellison et al. NEJM 2017

andere oplossingen

- (tijdelijk!) combineren

(lis + thiazide ± proximaal diureticum)

- continu infuus? roteren?

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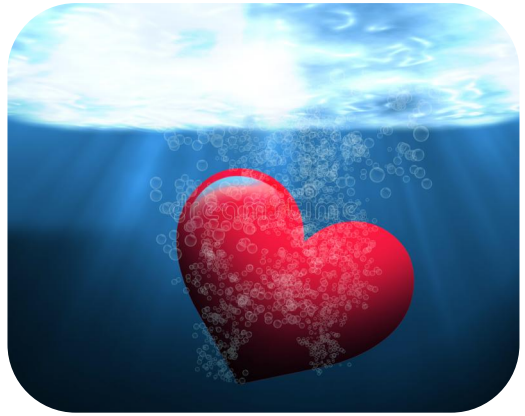

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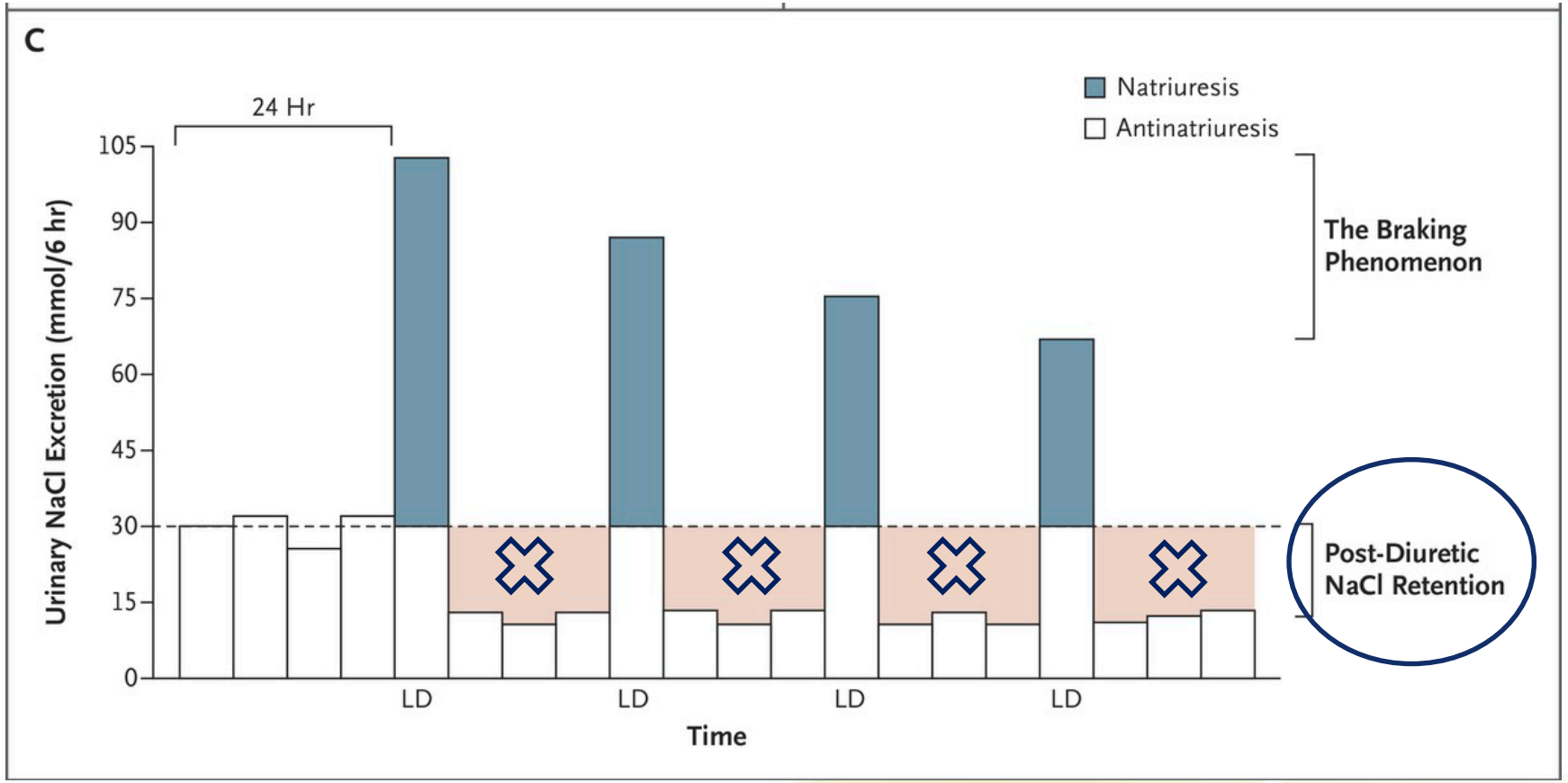
en nog problemen



meerdere toedieningen per dag
(ochtend + middag)

Ellison et al. NEJM 2017

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ambulante opvolging hartfalenpatiënt

- snel (< 1 week) en frequent
- diuretica: correcte onderhoudsdosis = ?
  - educatie patiënt: dyspnee en orthopnee, maar ook dehydratatie
  - dagelijks wegen

- bij symptomatische hypotensie: diureticum afbouwen?

- nierfunctie + ionogram ≥ 2x/jaar

- optitreren hartfalentherapie

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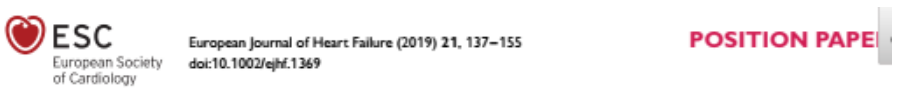
Er bestaan geen richtlijnen voor diuretica…


ESC European Society of Cardiology
European Journal of Heart Failure (2020)
doi:10.1002/ejhf.1697
POSITION PAPE

Evaluation of kidney function throughout the heart failure trajectory – a position statement from the Heart Failure Association of the European Society of Cardiology

Wilfried Mullens[1]*, Kevin Damman[2], Jeffrey M. Testani[3], Pieter Martens[1], Christian Mueller[4], Johan Lassus[5], W.H. Wilson Tang[6], Hadi Skouri[7], Frederik H. Verbrugge[8], Francesco Orso[9], Loreena Hill[10], Ural Dilek[11], Mitcha Lainscak[12], Patrick Rossignol[13], Marco Metra[14], Alexandre Mebazaa[15], Petar Seferovic[16], Frank Ruschitzka[17], and Andrew Coats[18]


ESC European Society of Cardiology
European Journal of Heart Failure (2019) 21, 137–155
doi:10.1002/ejhf.1369
POSITION PAPE

The use of diuretics in heart failure with congestion — a position statement from the Heart Failure Association of the European Society of Cardiology

Wilfried Mullens[1,2]*, Kevin Damman[3], Veli-Pekka Harjola[4], Alexandre Mebazaa[5], Hans-Peter Brunner-La Rocca[6], Pieter Martens[1,2], Jeffrey M. Testani[7], W.H. Wilson Tang[8], Francesco Orso[9], Patrick Rossignol[10], Marco Metra[11], Gerasimos Filippatos[12,13], Petar M. Seferovic[14], Frank Ruschitzka[15], and Andrew J. Coats[16]

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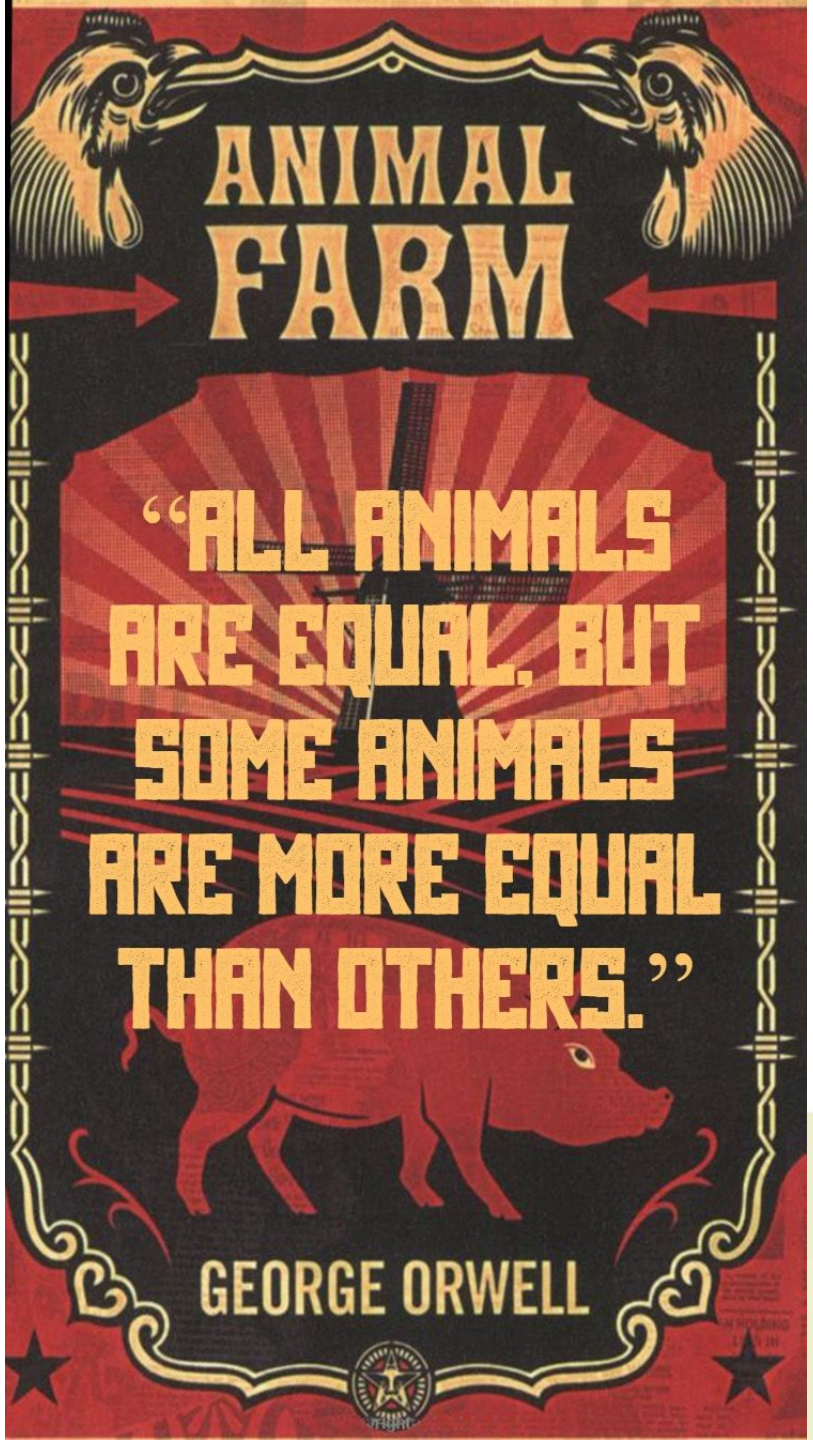

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Niet alle creatinine-stijgingen zijn gelijk

"pseudo –
worsening renal function"

efficiënte ontwatering bij acute decompensatie

opdrijven neurohormonale blokkade ("hartfalentherapie")

- geen slechtere prognose
- geen merkers van tubulaire schade
- louter weerspiegeling van renale hemodynamische veranderingen

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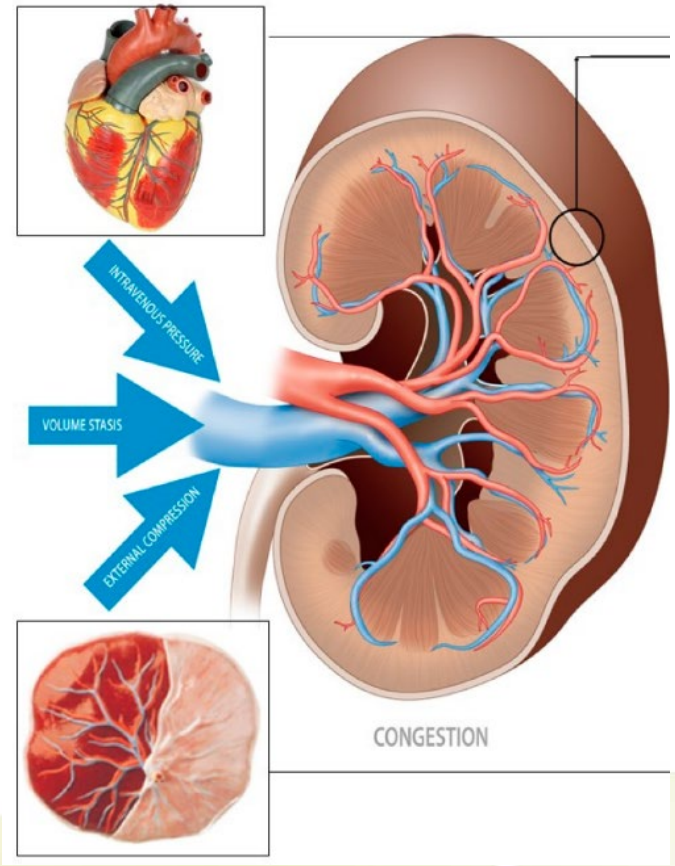

1. ontwateren doe je met lisdiuretica
2. hartfalen behandelen doe je met ACE-I / betablokker / ARNI / spiro
3. per oraal: bumetanide >> furosemide
4. liever 2x1 dan 1x2 (opsplitsen)
5. congestie is nefrotoxisch, niet het diureticum
6. slechtere nier = hogere dosis nodig
7. sluit intravasculaire ondervulling uit
8. vermijden NSAID's, zout en veel drinken
9. instrueer de patiënt (gewicht, diarree, hittegolf, …)
10. bij falen: verwijs voor IV therapie

heartfailurematters.org

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Angor pectoris: stent of medicatie?

Lessen uit de Ischemia Trial

Dr. Philippe Selleslagh

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Patient history

- 67 year old man
- 3/12 Hx: Chest tightness each time he walks up an incline, rushes for a bus or climbs 1 flight of stairs

- Hypertension, ex-smoker

Patient course

- Seen by primary physician, started on nitrates and aspirine 80 mg OD
- Referred to cardiology clinic:
  - CVS exam: normal

What next?

What is the diagnosis?

How should I treat the symptoms?

What is the risk to the patient?

How quickly do I need to treat?

What does the patient want?

What is the diagnosis?

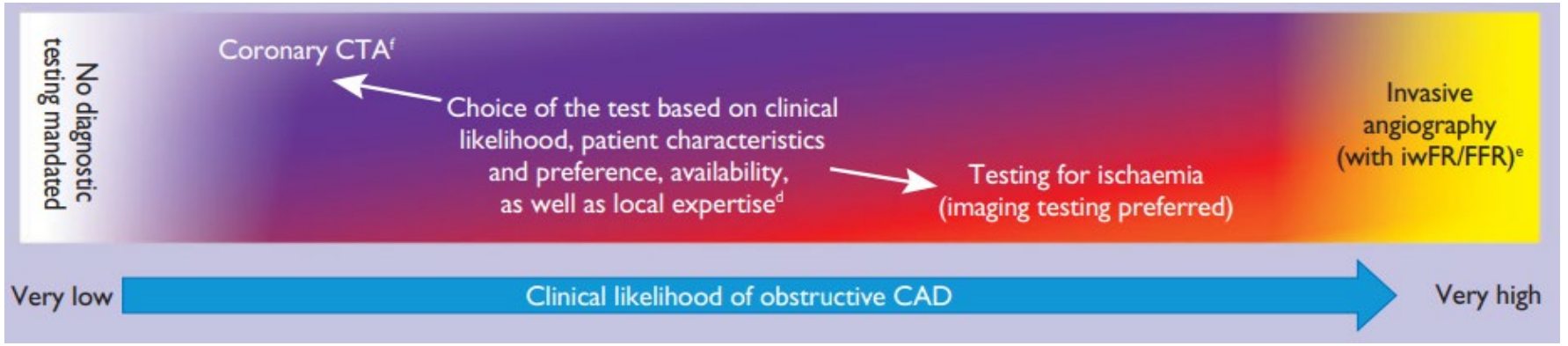
- Take a good history
- Consider pre-test probability of CAD

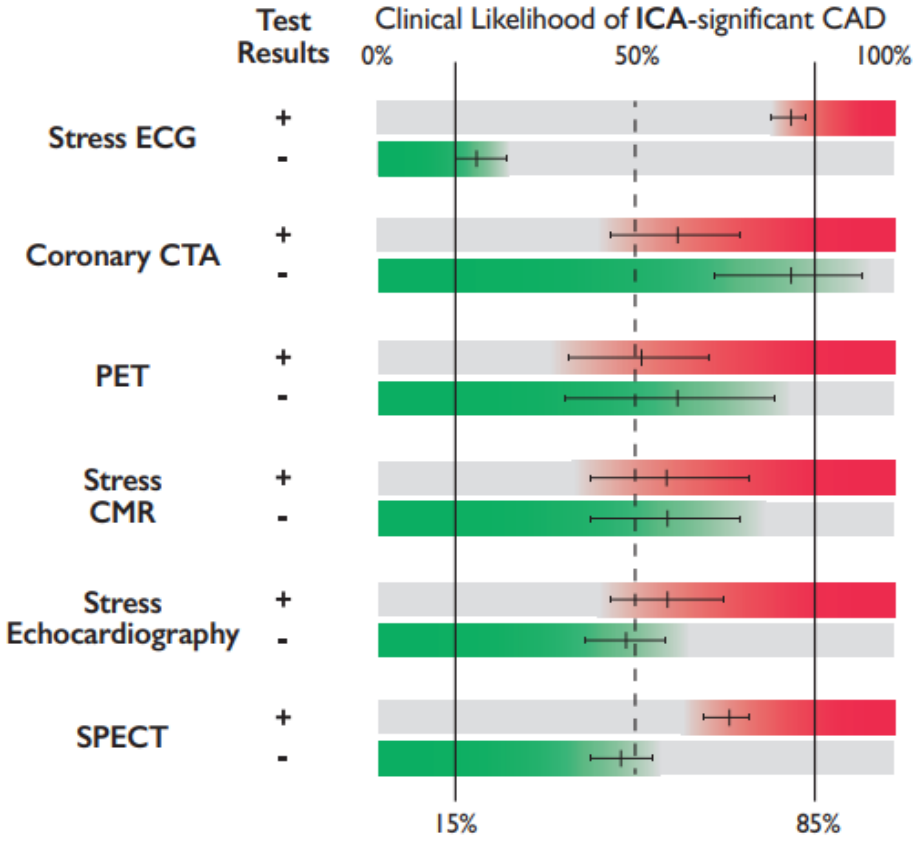
Table 5 **Pre-test probabilities of obstructive coronary artery disease in 15 815 symptomatic patients according to age, sex, and the nature of symptoms in a pooled analysis[64] of contemporary data[7,8,62]**

	Typical		Atypical		Non-anginal		Dyspnoea[a]	
Age	Men	Women	Men	Women	Men	Women	Men	Women
30–39	3%	5%	4%	3%	1%	1%	0%	3%
40–49	22%	10%	10%	6%	3%	2%	12%	3%
50–59	32%	13%	17%	6%	11%	3%	20%	9%
60–69	44%	16%	26%	11%	22%	6%	27%	14%
70+	52%	27%	34%	19%	24%	10%	32%	12%

CAD = coronary artery disease; PTP = pre-test probability.
[a]In addition to the classic Diamond and Forrester classes,[59] patients with dyspnoea only or dyspnoea as the primary symptom are included. The regions shaded dark green denote the groups in which non-invasive testing is most beneficial (PTP >15%). The regions shaded light green denote the groups with PTPs of CAD between 5–15%, in which testing for diagnosis may be considered after assessing the overall clinical likelihood based on the modifiers of PTPs presented in *Figure 3*.

- Further investigations for diagnosis and to asses risk





Clinical Likelihood range where test can **rule-in** CAD (Post-test probability will rise above 85%)

Clinical Likelihood range where test can **rule-out** CAD (Post-test probability will rise below 15%)

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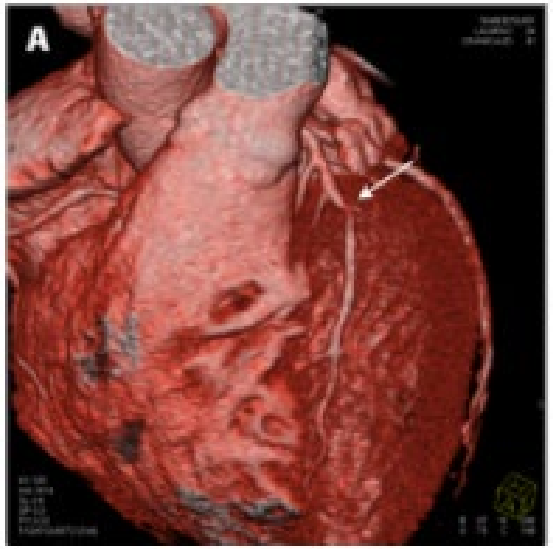

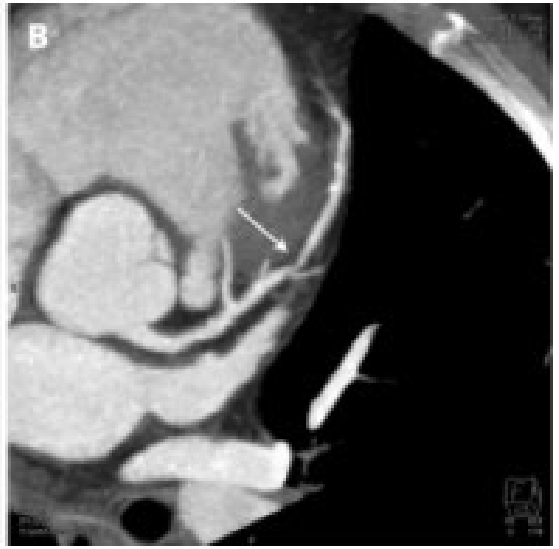

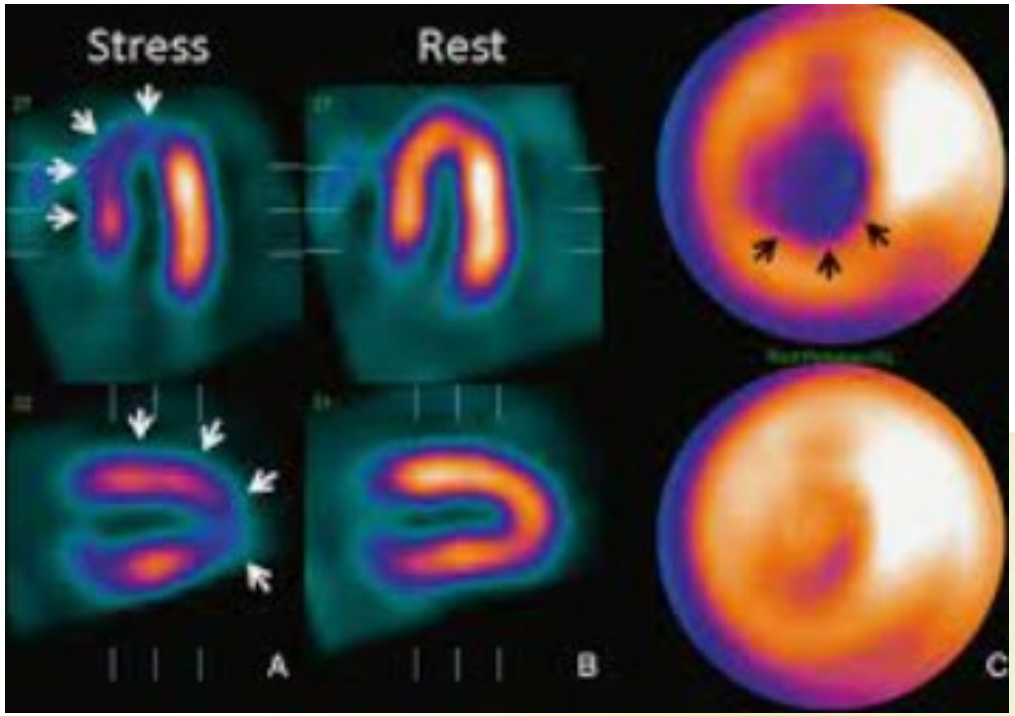

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Assessment of event risk

- Typical angina and LV systolic dysfunction in a pattern that indicates CAD

Table 6 Definitions of high event risk for different test modalities in patients with established chronic coronary syndromes[a] 102–104

Exercise ECG	Cardiovascular mortality >3% per year according to Duke Treadmill Score
SPECT or PET perfusion imaging	Area of ischaemia ≥10% of the left ventricle myocardium
Stress echocardiography	≥3 of 16 segments with stress-induced hypokinesia or akinesia
CMR	≥2 of 16 segments with stress perfusion defects or ≥3 dobutamine-induced dysfunctional segments
Coronary CTA or ICA	Three-vessel disease with proximal stenoses, LM disease, or proximal anterior descending disease
Invasive functional testing	FFR ≤0.8, iwFR ≤0.89

CTA = computed tomography angiography; CMR = cardiac magnetic resonance; ECG = electrocardiogram; FFR = fractional flow reserve; ICA = invasive coronary angiography; iwFR = instantaneous wave-free ration (instant flow reserve); LM = left main; PET = positron emission tomography; SPECT; single-photon emission computed tomography.
[a]For detailed explanations, refer to the Supplementary Data.

2018 ESC/EACTS guidelines for myocardial revascularization

Indications for revascularization in CCS

For prognosis — Class I

Left main disease*

Proximal LAD*

2VD or 3VD and LVEF ≤35%*

Large area of ischemia or FFR+**

Single remaining patent artery

For symptoms — Class I

Haemodynamically significant coronary stenosis* in the presence of limiting angina or angina equivalent, with insufficient response to optimized medical therapy, In consideration of patient compliance and wishes in relation to the intensity of anti-anginal therapy

* with stenosis >50% and documented ischaemia or a hemodynamically relevant lesion defined by FFR ≤0.80 or iwFR ≤0.89, or >90% stenosis in a major coronary vessel.
** based on FFR <0.75 indicating a prognostically relevant lesion.

Extent of CAD (anatomical and/or functional)		Class	Level
For prognosis	Left main disease with stenosis >50%.[a]	I	A
	Proximal LAD stenosis >50%.[a]	I	A
	Two- or three-vessel disease with stenosis >50% with impaired LV function (LVEF ≤35%)[a]	I	A
	Large area of ischaemia detected by functional testing (>10% LV) or abnormal invasive FFR[b]	I	B
	Single remaining patent coronary artery with stenosis >50%.	I	C

[a] With documented ischaemia or haemodynamically relevant lesion defined by FFR ≤ 0.80 or iwFR ≤ 0.89 or > 90% stenosis in a major coronary vessel

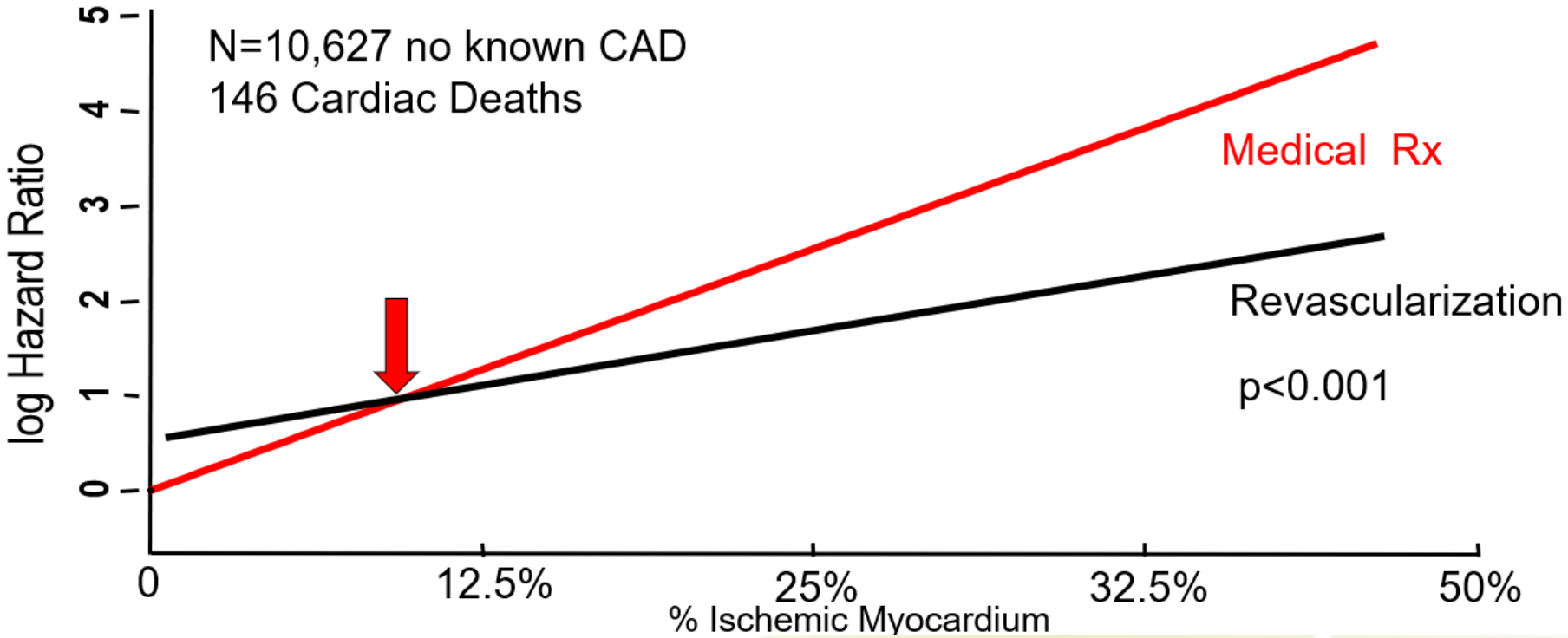
[b] Based on FFR < 0.75 indicating a prognostically relevant lesion

It is sobering to realize that among patients undergoing angiography, the guideline-based indications for revascularization with the objective of prolonging survival are driven by the categorization of disease severity and left ventricular function established by the three original trials of bypass surgery vs. medical therapy ~30 years ago.

Bernard J. Gersh [1]* and **Deepak L. Bhatt** [2]

[1]Department of Cardiovascular Medicine, Mayo College of Medicine, Mayo Clinic, 200 First Street, SW, Rochester, MN 55905, USA; and [2]Department of Cardiovascular Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Observational study: Revascularization was associated with lower risk of cardiac death only in those with >10% ischemia on perfusion imaging



Hachamovitch Circulation 2003;107:2900-2907.

The NEW ENGLAND JOURNAL of MEDICINE

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Initial Invasive or Conservative Strategy for Stable Coronary Disease

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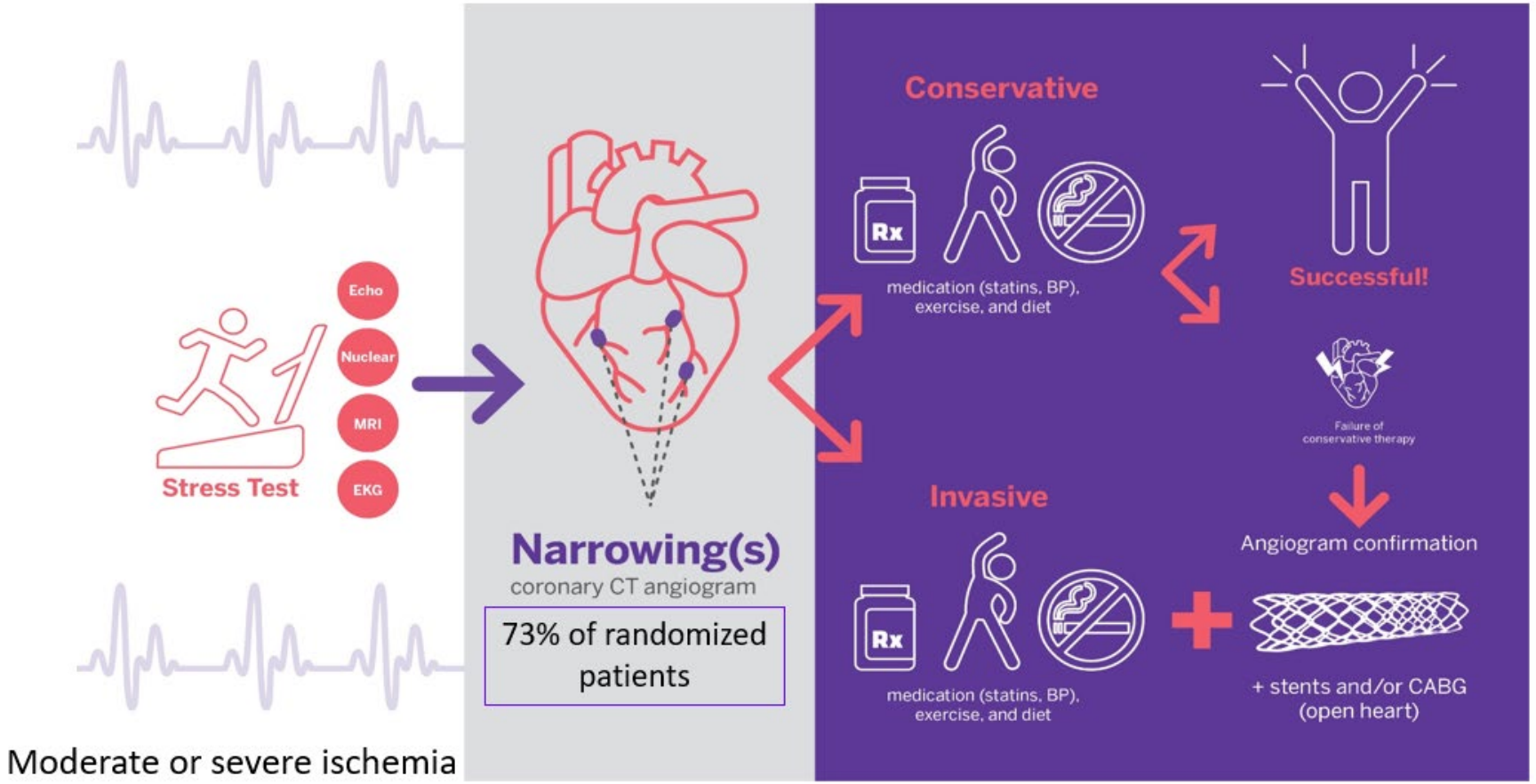
In stable patients with at least moderate ischemia on a stress test, is there a benefit to adding cardiac catheterization and, if feasible, revascularization to optimal medical therapy?

Limitations of Prior Trials

- Selection bias (randomization occurred after cath)
- No minimum threshold of ischemia required
- DES not used in COURAGE and BARI 2D*
- PCI not FFR-guided in COURAGE and BARI 2D
- CABG not done in COURAGE or FAME 2

* DES only used in a small percentage of participants.

ISCHEMIA design overview



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Endpoints

Primary Endpoint:

- Time to CV death, MI, hospitalization for unstable angina, heart failure or resuscitated cardiac arrest

Major Secondary Endpoints:

- Time to CV death or MI
- Quality of Life

Other Endpoints include:

- All-Cause Death
- Net clinical benefit (stroke added to primary endpoint)
- Components of primary endpoint

Eligibility Criteria

Clinical and Stress Test Eligibility Criteria

Inclusion Criteria

- Age ≥21 years
- Moderate or severe ischemia*
  - Nuclear ≥10% LV ischemia (summed difference score ≥7)
  - Echo ≥3 segments stress-induced moderate or severe hypokinesis, or akinesis
  - CMR
    - Perfusion: ≥12% myocardium ischemic, and/or
    - Wall motion: ≥3/16 segments with stress-induced severe hypokinesis or akinesis
  - Exercise Tolerance Testing (ETT) ≥1.5mm ST depression in ≥2 leads or ≥2mm ST depression in single lead at <7 METS, with angina

Major Exclusion Criteria

- NYHA Class III-IV HF
- Unacceptable angina despite medical therapy
- EF < 35%
- ACS within 2 months
- PCI or CABG within 1 year
- eGFR <30 mL/min or on dialysis

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Eligibility Criteria

CCTA Eligibility Criteria

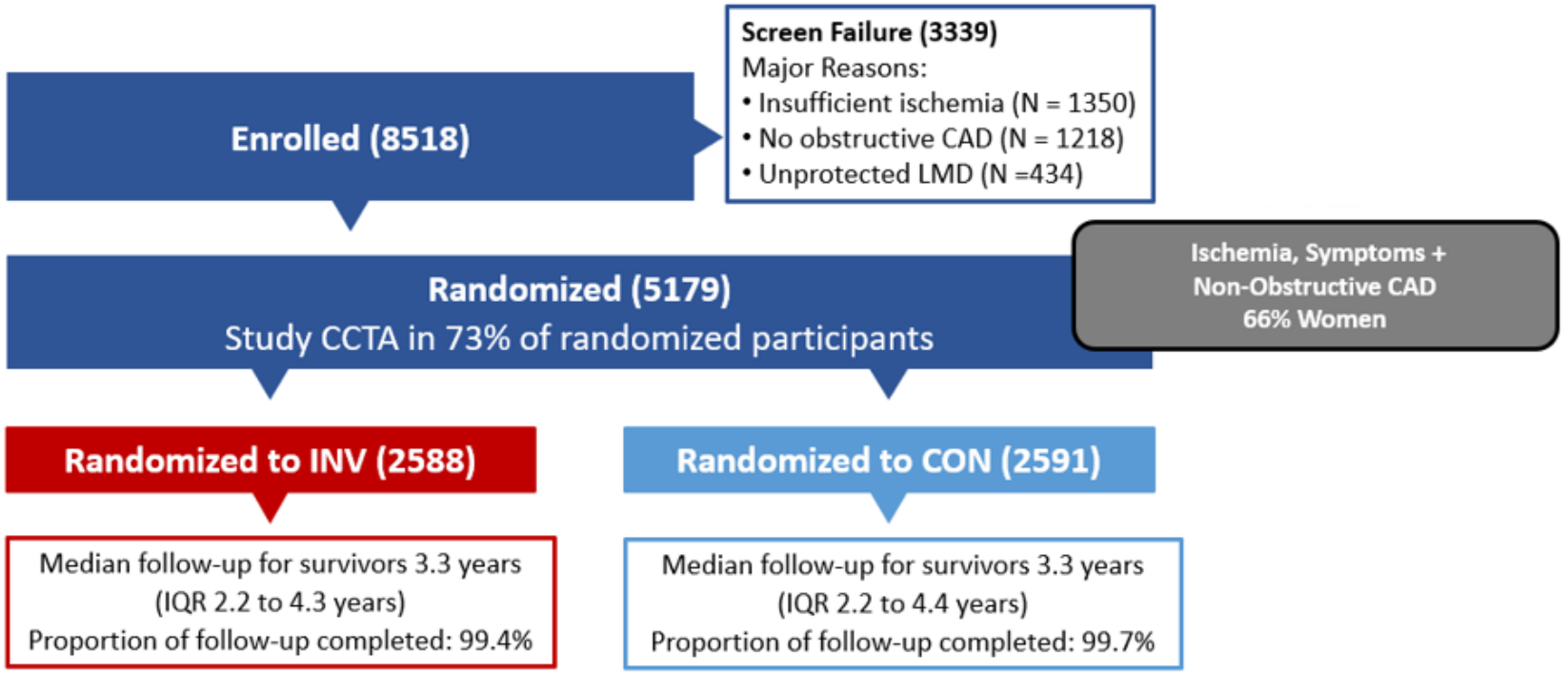
Inclusion Criteria

- ≥50% stenosis in a major epicardial vessel (stress imaging participants)
- ≥70% stenosis in a proximal or mid vessel (ETT participants)

Major Exclusion Criteria

- ≥50% stenosis in unprotected left main

Study Flow



Baseline Characteristics

Characteristic	Total	INV	CON
Clinical			
Age at Enrollment (yrs.)			
Median	64 (58, 70)	64 (58, 70)	64 (58, 70)
Female Sex (%)	23	23	22
Hypertension (%)	73	73	73
Diabetes (%)	42	41	42
Prior Myocardial Infarction (%)	19	19	19
Ejection Fraction, Median (%) (n=4637)	60 (55, 65)	60 (55, 65)	60 (55, 65)
Systolic Blood Pressure, Median (mmHg)	130 (120, 142)	130 (120, 142)	130 (120, 142)
Diastolic Blood Pressure, Median (mmHg)	77 (70, 81)	77 (70, 81)	77 (70, 81)
LDL Cholesterol, Median (mg/dL)	83 (63, 111)	83 (63, 111)	83 (63, 109.5)
History of Angina	90%	90%	89%
Angina Began or Became More Frequent Over the Past 3 Months	29%	29%	29%
Stress Test Modality			
Stress Imaging (%)	75	75	76
Exercise Tolerance Test (ETT) (%)	25	25	24

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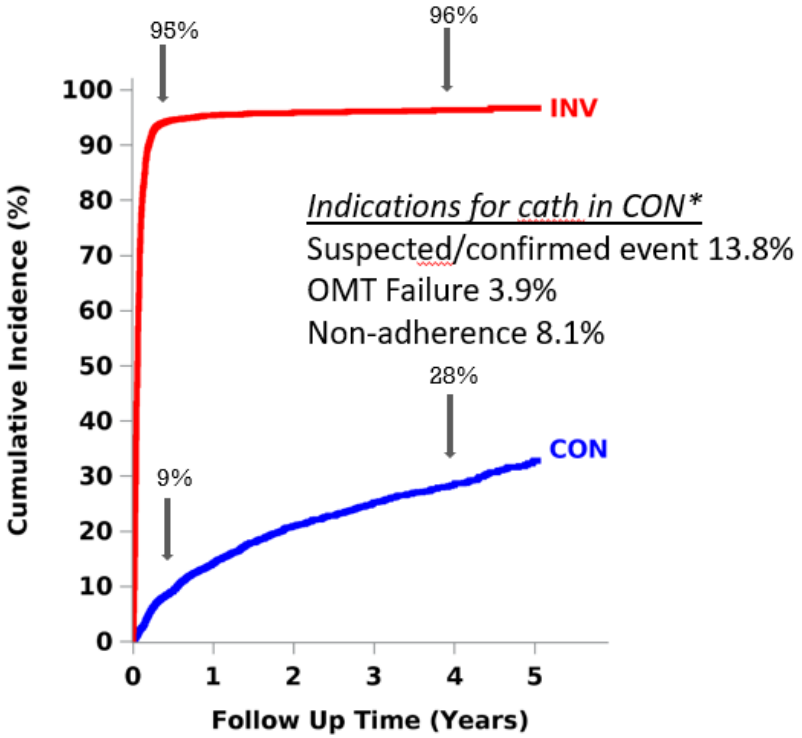
Cardiac Catheterization and Revascularization

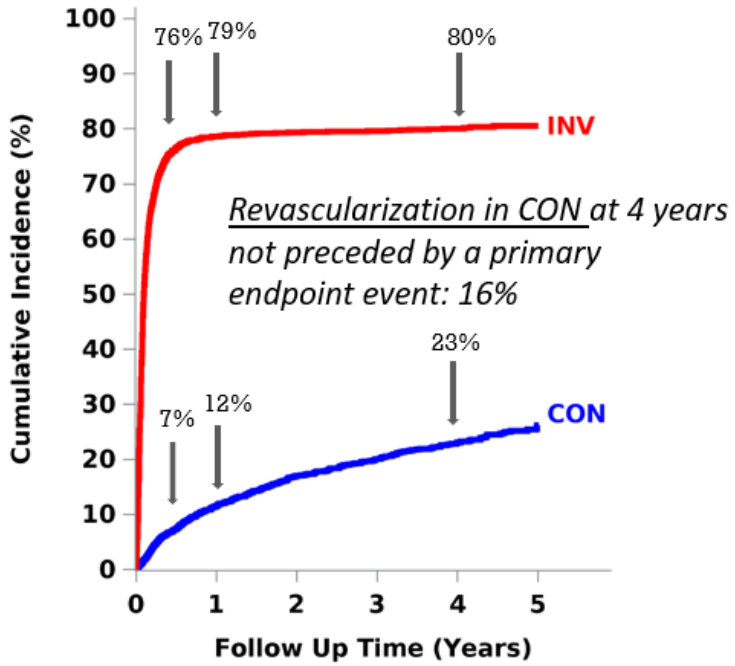
Cardiac Catheterization



*Indications for cath in CON**
Suspected/confirmed event 13.8%
OMT Failure 3.9%
Non-adherence 8.1%

CON	2591	2186	1646	1087	601	232
INV	2588	111	79	50	20	4

Revascularization



Revascularization in CON at 4 years not preceded by a primary endpoint event: 16%

CON	2591	2250	1721	1157	642	254
INV	2588	523	410	289	155	54

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Mode of Revascularization

First Procedure for Those Revascularized in Invasive Group (80% of INV)

Of the 20% with no revascularization
~2/3 had insignificant disease on coronary angiogram
~1/3 had extensive disease unsuitable for any mode of revascularization

First Procedure	Total
PCI	74%
• Successful, stent able to be placed	93%
• Of stents placed, drug eluting	98%

First Procedure	Total
CABG	26%
• Arterial Grafts	93%
• IMA	92%

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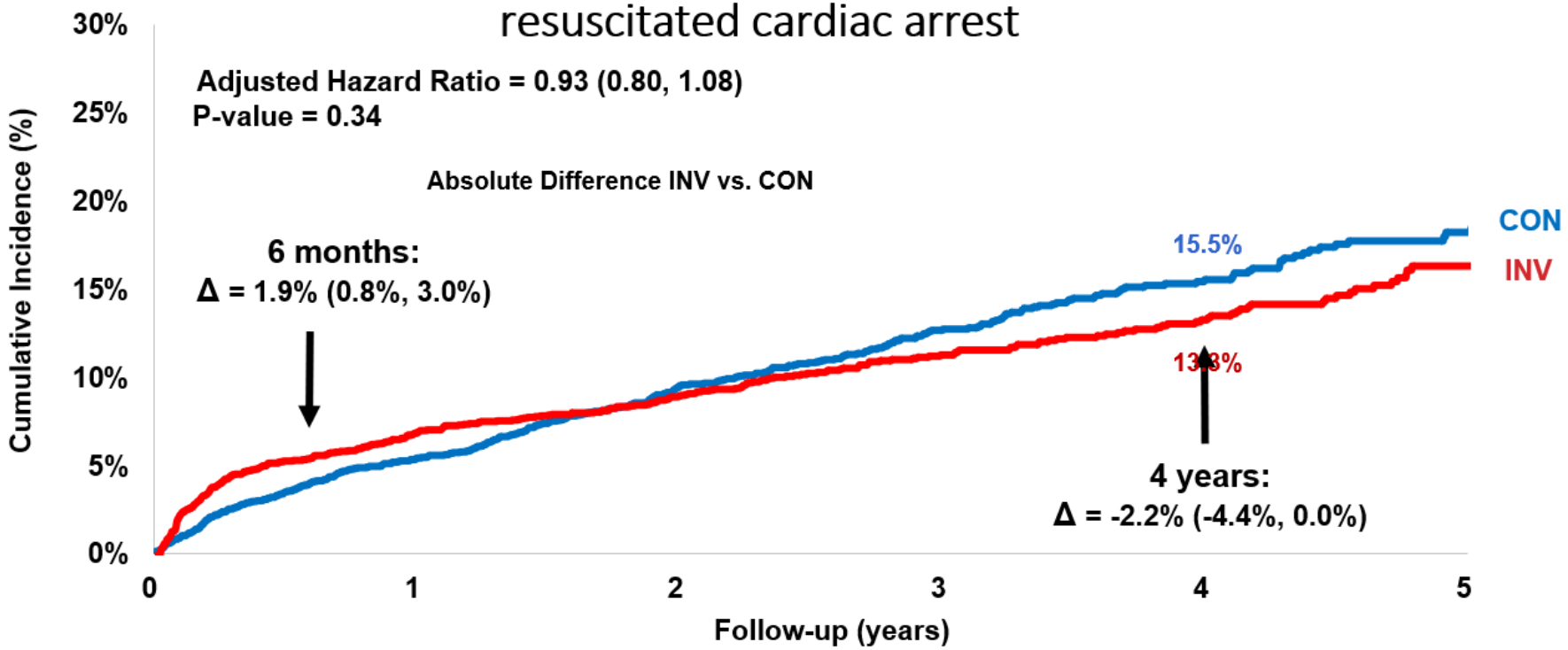
Primary Outcome: CV Death, MI, hospitalization for UA, HF or resuscitated cardiac arrest



Subjects at Risk

CON	2591	2431	1907	1300	733	293
INV	2588	2364	1908	1291	730	271

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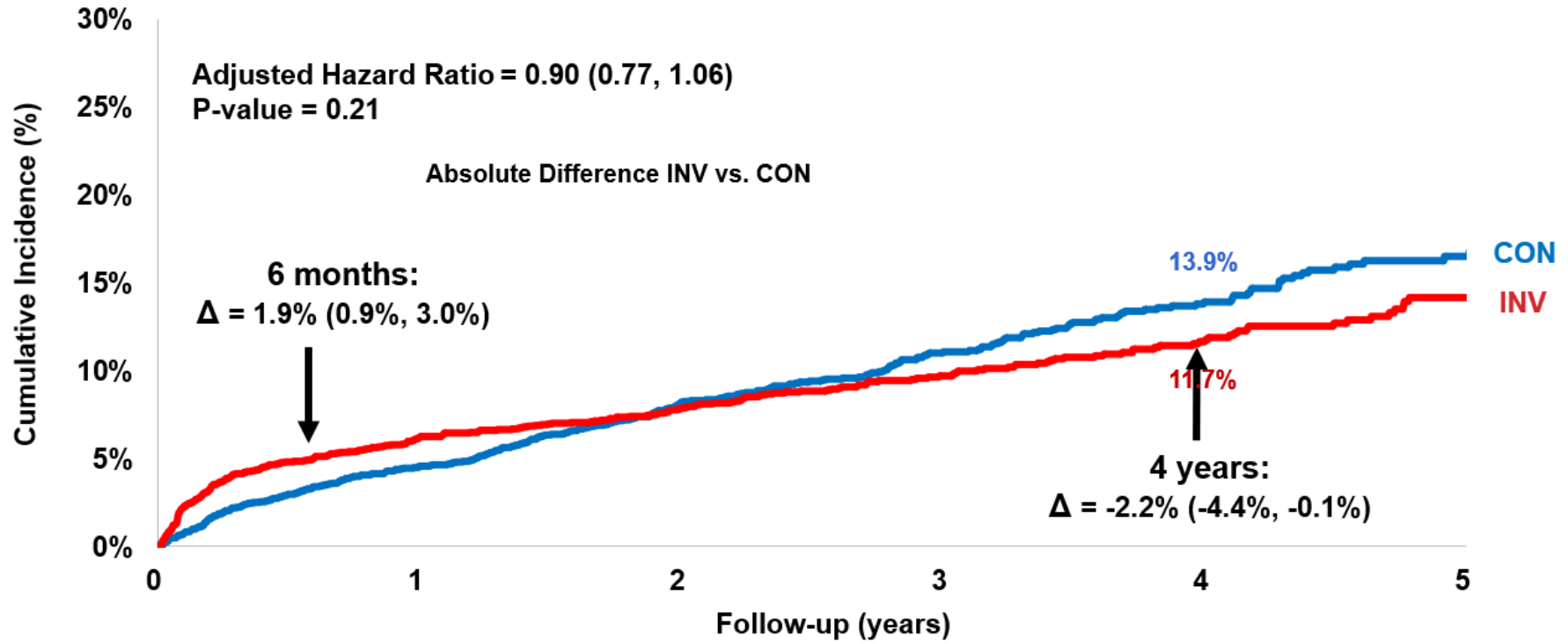
Major Secondary: CV Death or MI



Subjects at Risk

CON	2591	2453	1933	1325	746	298
INV	2588	2383	1933	1314	752	282

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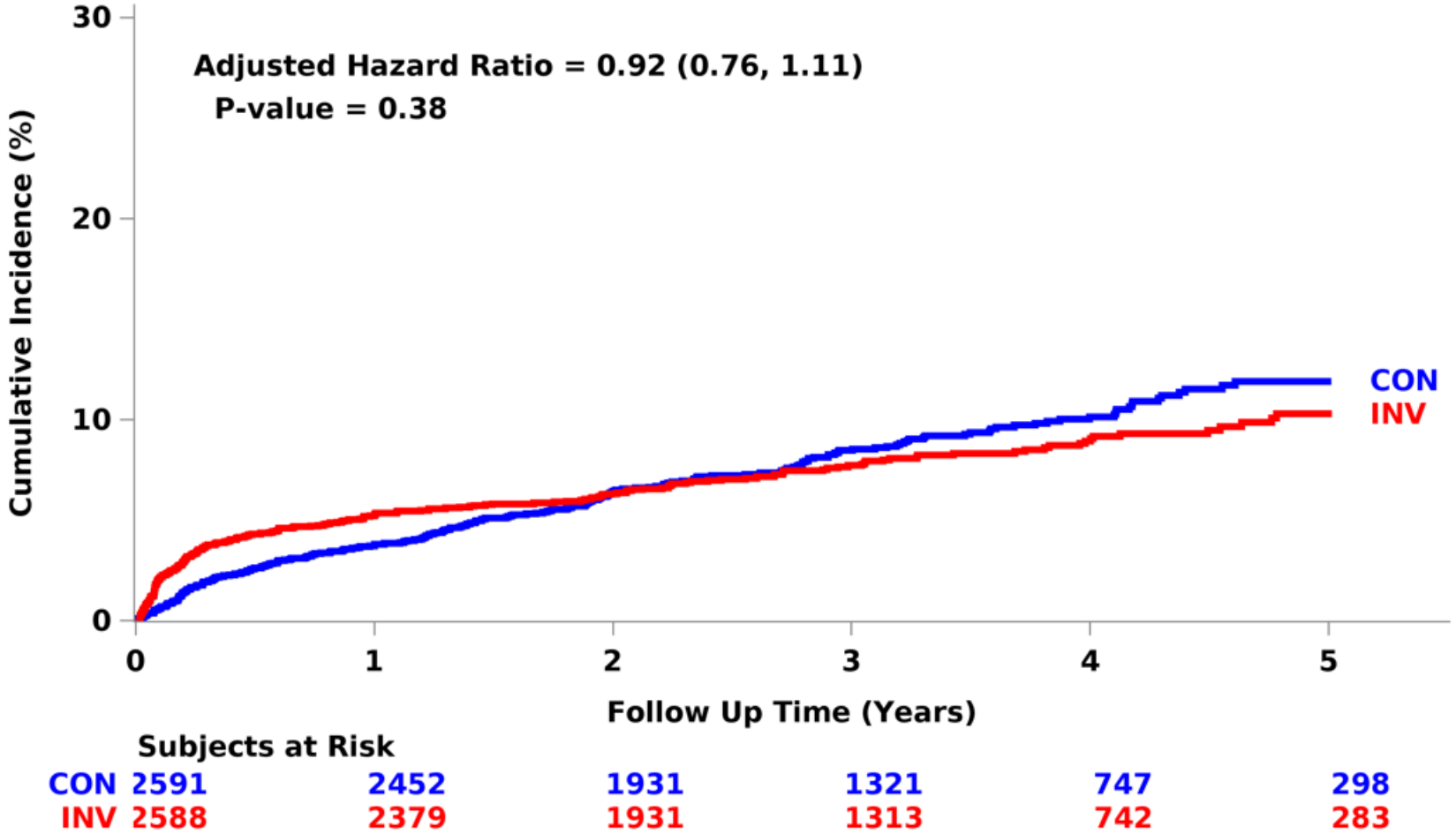
Myocardial Infarction



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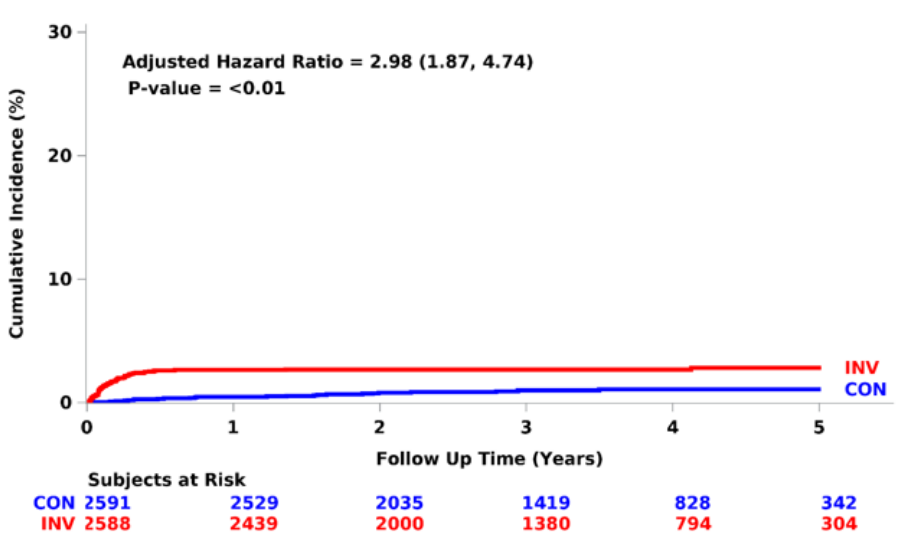
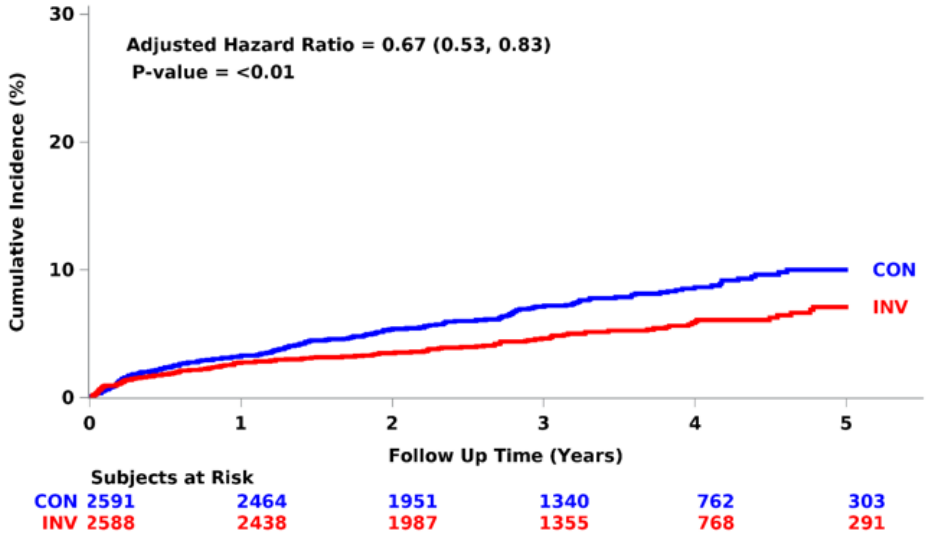
Procedural MI
Type 4a or 5 MI



Spontaneous MI
Types 1, 2, 4b, or 4c MI



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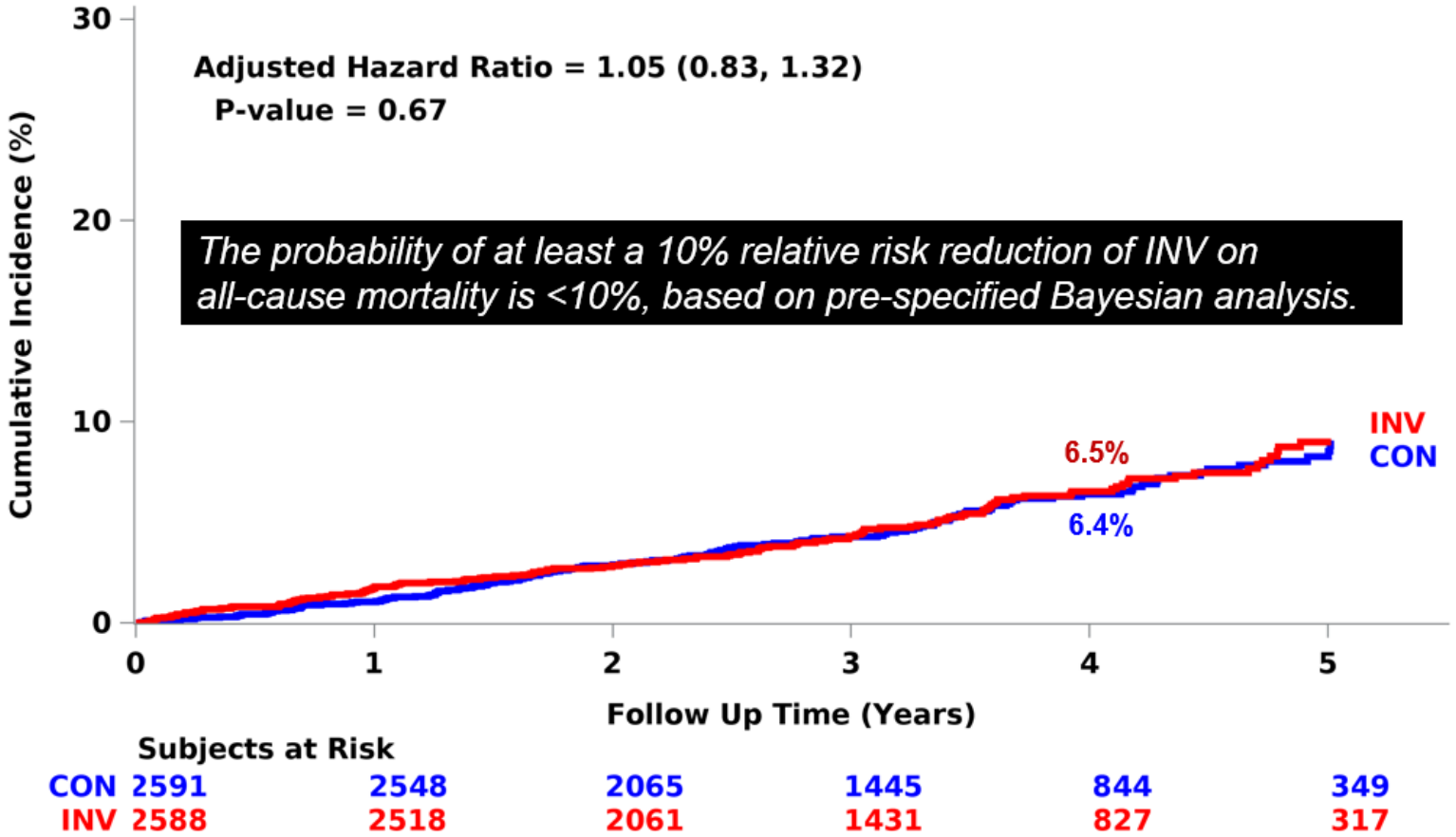
All-Cause Death



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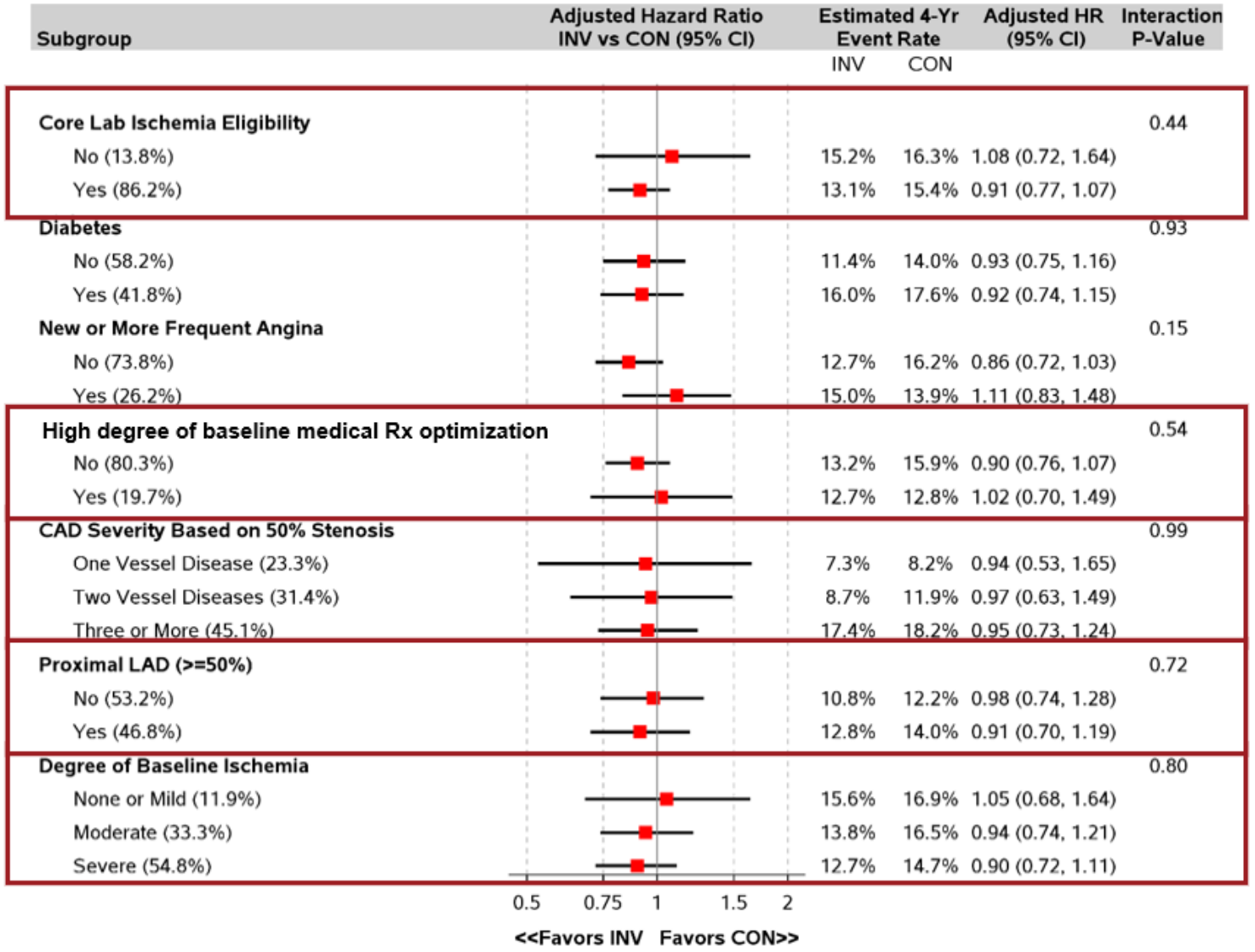
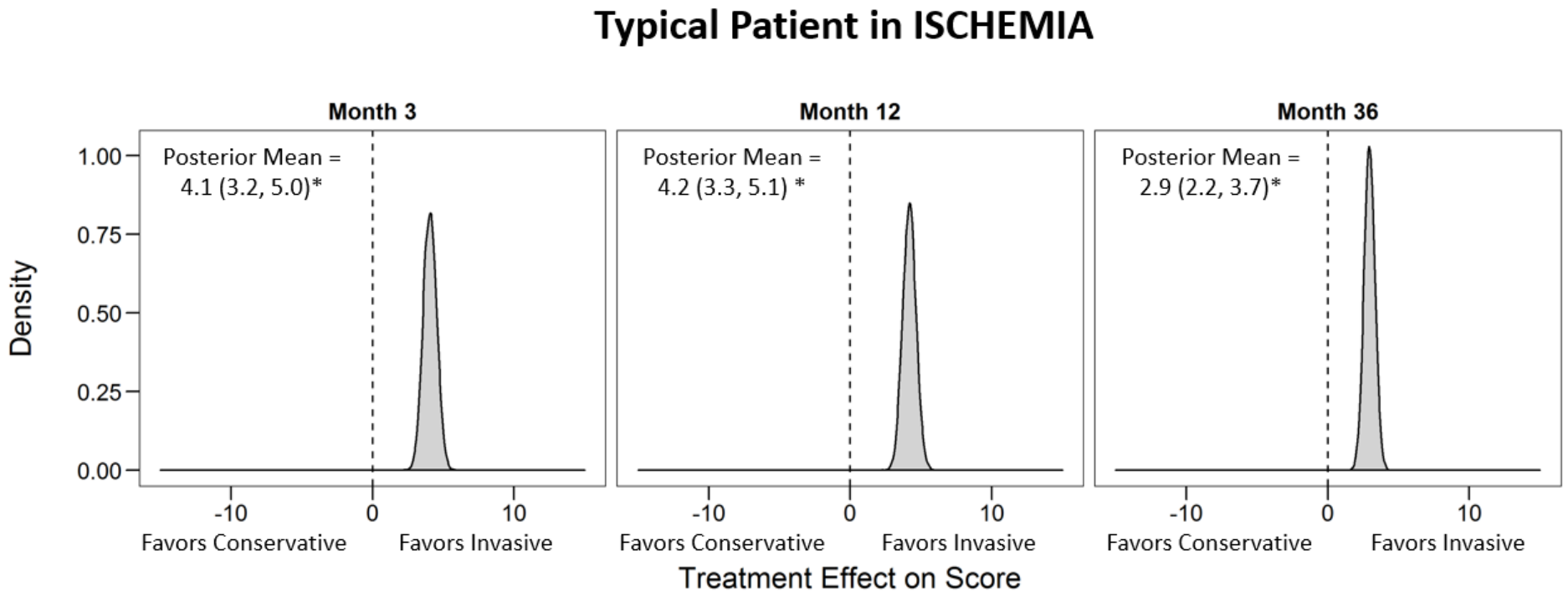
Primary endpoint
Pre-specified Important Subgroups
There was no heterogeneity of treatment effect



Subgroup	Adjusted Hazard Ratio INV vs CON (95% CI)	Estimated 4-Yr Event Rate INV	Estimated 4-Yr Event Rate CON	Adjusted HR (95% CI)	Interaction P-Value
Core Lab Ischemia Eligibility					0.44
No (13.8%)		15.2%	16.3%	1.08 (0.72, 1.64)	
Yes (86.2%)		13.1%	15.4%	0.91 (0.77, 1.07)	
Diabetes					0.93
No (58.2%)		11.4%	14.0%	0.93 (0.75, 1.16)	
Yes (41.8%)		16.0%	17.6%	0.92 (0.74, 1.15)	
New or More Frequent Angina					0.15
No (73.8%)		12.7%	16.2%	0.86 (0.72, 1.03)	
Yes (26.2%)		15.0%	13.9%	1.11 (0.83, 1.48)	
High degree of baseline medical Rx optimization					0.54
No (80.3%)		13.2%	15.9%	0.90 (0.76, 1.07)	
Yes (19.7%)		12.7%	12.8%	1.02 (0.70, 1.49)	
CAD Severity Based on 50% Stenosis					0.99
One Vessel Disease (23.3%)		7.3%	8.2%	0.94 (0.53, 1.65)	
Two Vessel Diseases (31.4%)		8.7%	11.9%	0.97 (0.63, 1.49)	
Three or More (45.1%)		17.4%	18.2%	0.95 (0.73, 1.24)	
Proximal LAD (>=50%)					0.72
No (53.2%)		10.8%	12.2%	0.98 (0.74, 1.28)	
Yes (46.8%)		12.8%	14.0%	0.91 (0.70, 1.19)	
Degree of Baseline Ischemia					0.80
None or Mild (11.9%)		15.6%	16.9%	1.05 (0.68, 1.64)	
Moderate (33.3%)		13.8%	16.5%	0.94 (0.74, 1.21)	
Severe (54.8%)		12.7%	14.7%	0.90 (0.72, 1.11)	

Primary Outcome: Benefit of Invasive Rx on SAQ Summary Score



**95% Highest Posterior Density Interval*

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Summary

- The curves cross for the primary endpoint and the major secondary endpoint at approximately 2 years from randomization
  - ~2 in 100 *higher* estimated rate with INV at 6 months
  - ~2 in 100 *lower* estimated rate with INV at 4 years
- Procedural MIs were increased with an invasive strategy
- Spontaneous MIs were reduced with an invasive strategy
- Low all-cause mortality in both groups despite high-risk clinical characteristics, high-risk ischemia and extensive CAD
- No heterogeneity of treatment effect, including by type of stress test, severity of ischemia or extent of CAD
- Very low rates of procedure-related stroke and death

Summary

- Patients with stable CAD and moderate to severe ischemia had significant, durable improvements in angina control and quality of life with an invasive strategy *if they had angina* (daily/weekly or monthly)

- In patients without angina, an invasive strategy led to minimal symptom or quality of life benefits, as compared with a conservative strategy

- In patients with angina, shared decision-making should occur to align treatment with patients' goals and preferences

2018 ESC/EACTS guidelines for myocardial revascularization

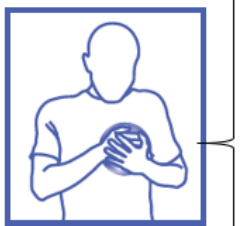
Indications for revascularization in CCS

	Class	Level	Valid after the ISCHEMIA trial?
Left main disease with stenosis >50%*	I	A	**Yes**, left main disease was excluded
Proximal LAD stenosis >50%*	I	A	**Maybe not**: proximal LAD was not a treatment modifier
Two- or three-vessel disease with stenosis >50% with impaired LV function (LVEF ≤35%)*	I	A	**Yes**, patients with LVEF <35% were excluded
Large area of ischaemia detected by functional testing (>10% LV) or abnormal invasive FFR**	I	B	**Maybe not**: severe ischaemia was included and FFR was allowed
Single remaining patent coronary artery with stenosis >50%*	I	C	**Maybe**: no clues from the trial

* With documented ischaemia or a haemodynamically relevant lesion defined by FFR ≤0.80 or iwFR ≤0.89, or >90% stenosis in a major coronary vessel. ** Based on FFR <0.75 indicating a prognostically relevant lesion

Next guidelines for myocardial revascularization

How I would frame the new recommendation



Angina

Infrequent, acceptable

Conservative strategy
Class I

OMT and lifestyle modification

If ISCHEMIA-like characteristics

ISCHEMIA-like?
- Exclude ACS, NYHA III/IV
- Exclude LMCA (CCTA)
- Exclude LVEF <35% (echo)
- Exclude ANOCA/INOCA (CCTA, SPECT)

Monitor response to treatment. In case of failure of the conservative strategy, move to the invasive strategy
Class I

If LMCA disease is suspected or confirmed
If LVEF<35% of likely coronary cause

Frequent, unacceptable

Invasive strategy
Class I

OMT and lifestyle modification.
Coronary angiography and revascularization

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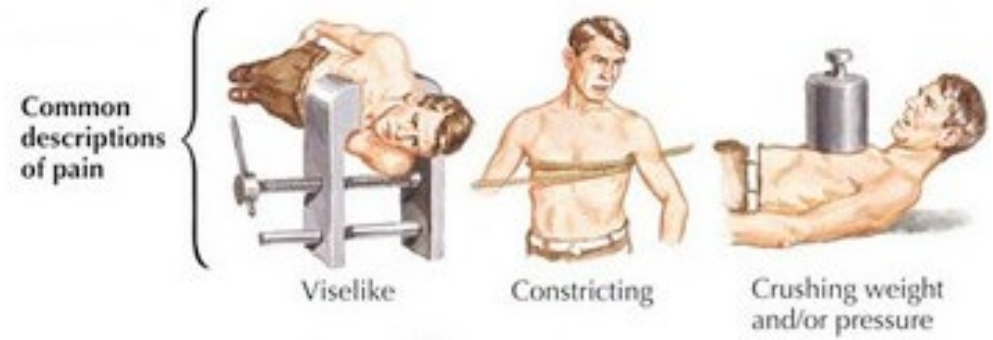
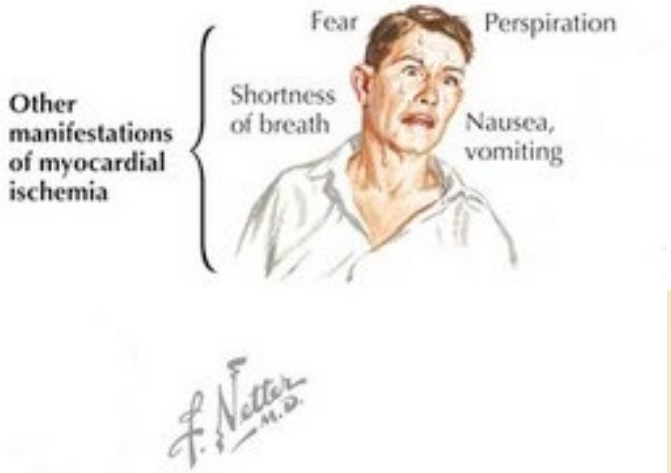
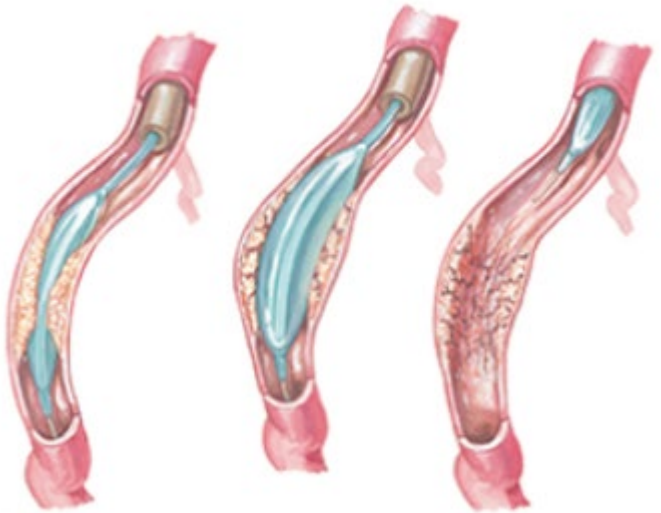
What does the patient want?





The end



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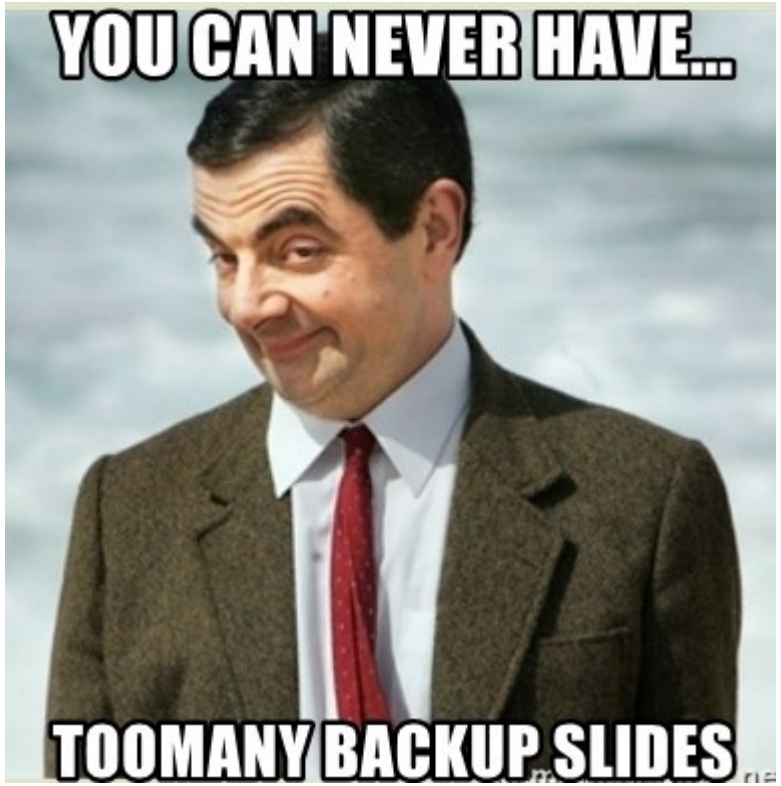
Backup slides



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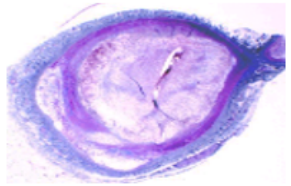
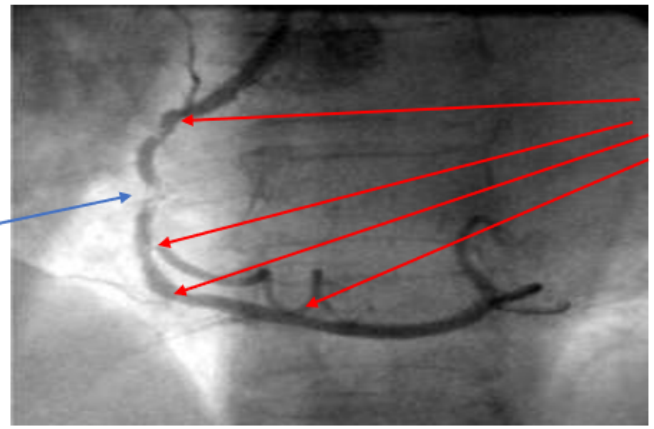
A paradigm that suggests why randomized trials have not demonstrated a survival benefit for revascularization in SIHD

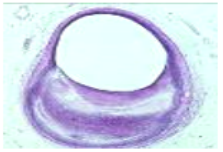
Severe Obstruction (angina, no rupture) vs Mild Obstruction (no angina, likely to rupture)

Severe fibrotic plaque
- **Severe obstruction**
- **No lipid**
- **Fibrosis, Ca^{2+}**





Vulnerable plaque
- **Minor obstruction**
- **Eccentric plaque**
- **Lipid pool**
- **Thin cap**

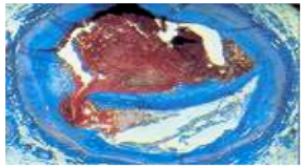


Plaque rupture
- **Acute MI**
- **Unstable angina**
- **Sudden death**

Exertional angina
- **(+) ETT**

Revascularization
Anti-anginal Rx

Pharmacologic stabilization
Early identification of high-risk?



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International Study of Comparative Health Effectiveness with Medical and Invasive Approaches - Chronic Kidney Disease

- In stable patients with advanced CKD and at least moderate ischemia on a stress test, is there a benefit to adding cardiac catheterization and, if feasible, revascularization to optimal medical therapy?

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CKD Patients are Under-Represented in Contemporary Revascularization vs. Medicine SIHD Trials

2007

COURAGE

eGFR <30: 16 Subjects

2009

BARI 2D

A WINDOW OF OPPORTUNITY FOR COORDINATED CARE

Subjects with serum Cr >2 mg/dl excluded

2012

FAME 2 Trial

Serum Cr >2 mg/dl: 20 subjects

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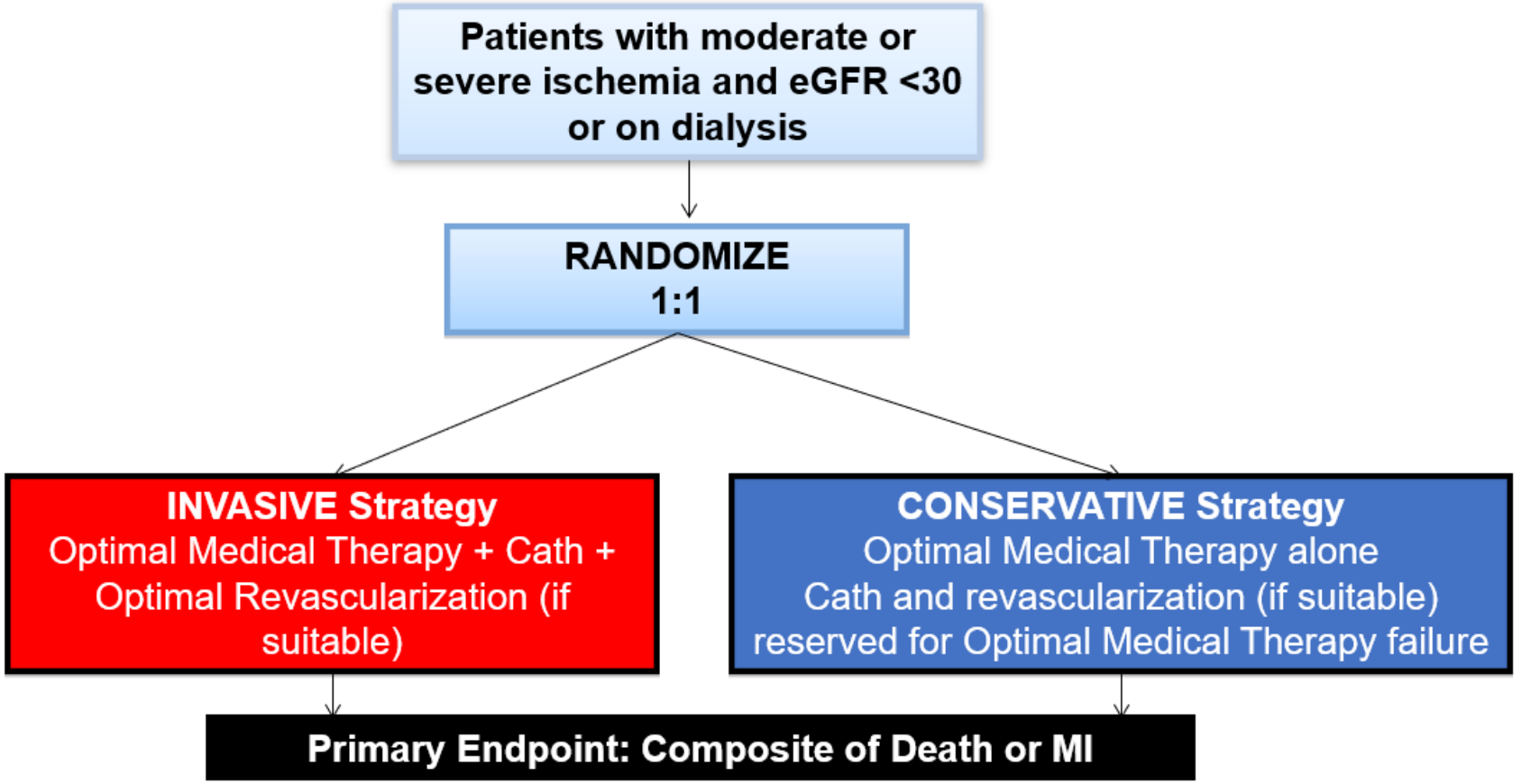
Study Design



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Eligibility Criteria

Key Inclusion Criteria

- At least moderate ischemia on an exercise or pharmacologic stress test (site determined)
- End-stage renal disease on dialysis or estimated glomerular filtration rate (eGFR) <30mL/min/1.73m^2

Key Exclusion Criteria

- Left ventricular ejection fraction <35%
- NYHA class III-IV heart failure
- Unacceptable level of angina despite maximal medical therapy
- ACS within the previous 2 months
- PCI or CABG within the previous 12 months

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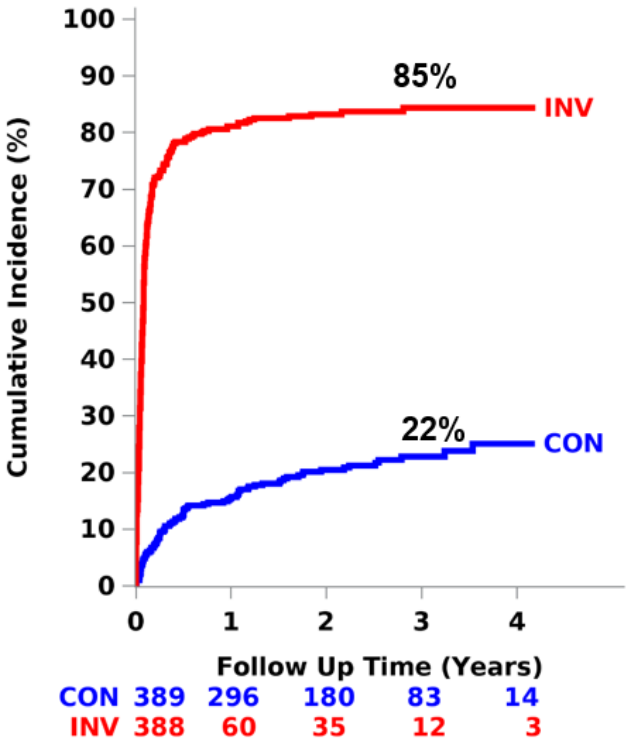
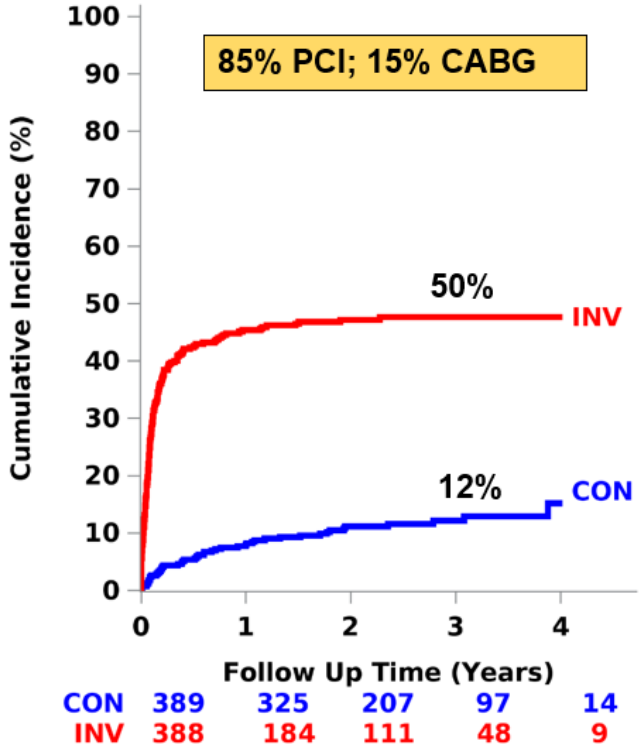
Coronary Angiography and Revascularization*

Coronary Angiography



Revascularization



*Not preceded by endpoint event

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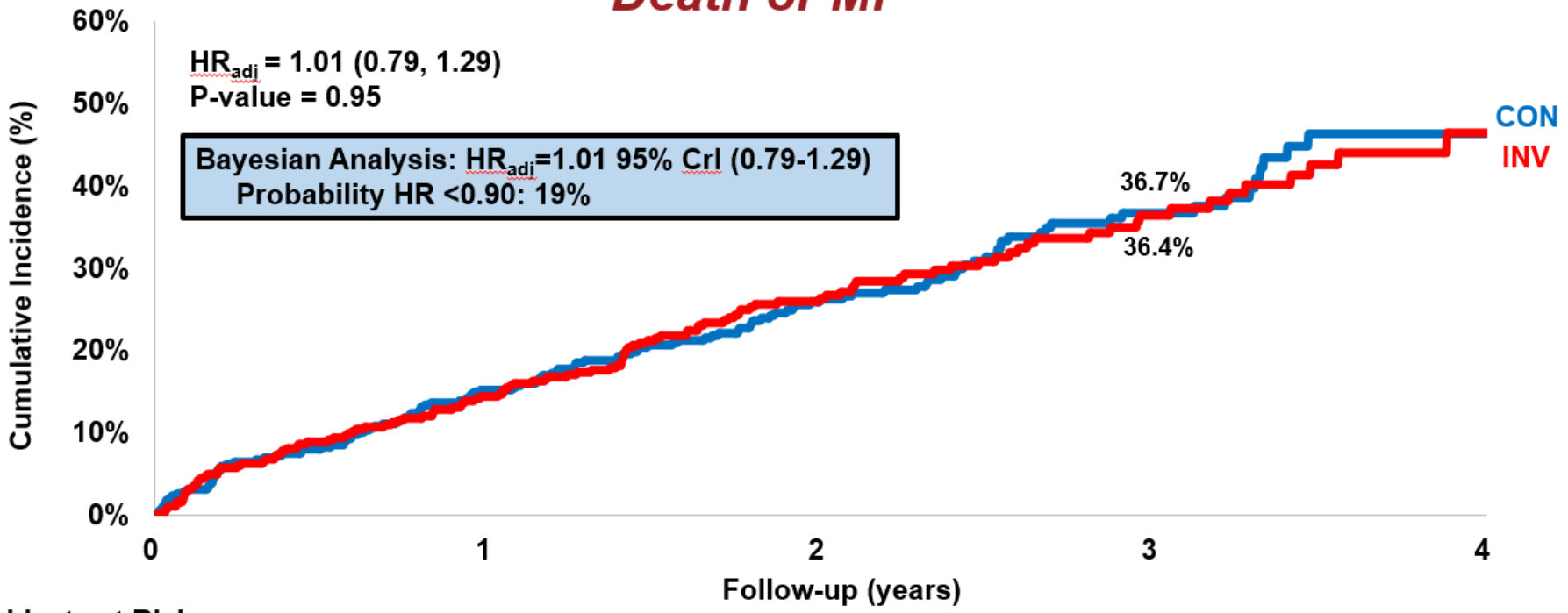
Primary End Point

Death or MI



Subjects at Risk

CON	389	330	213	91	13
INV	388	323	190	80	18

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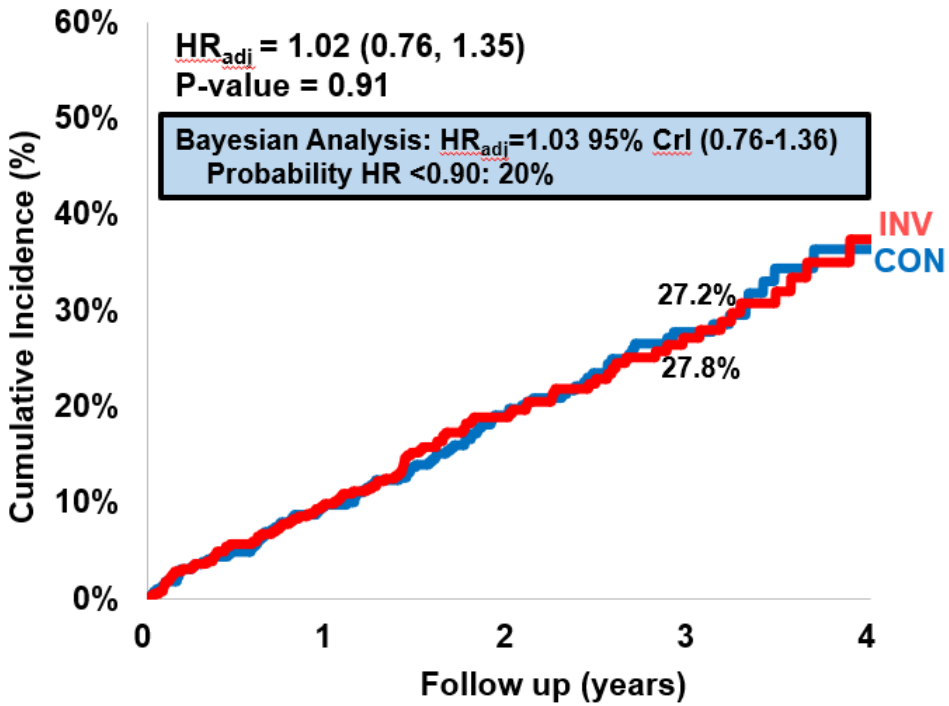
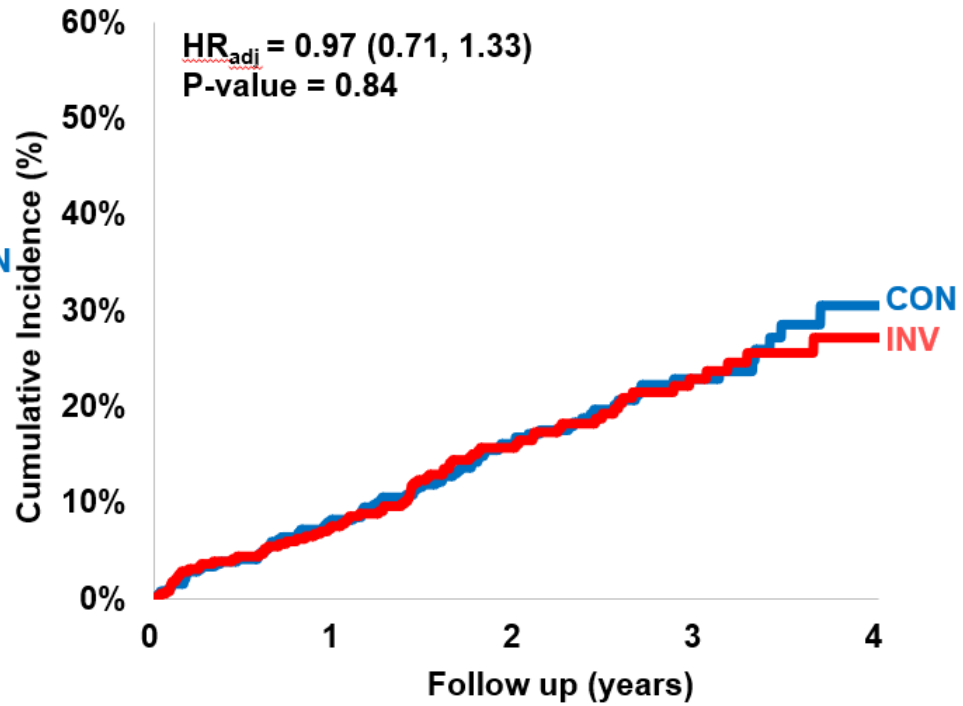
Secondary End Points

Death



CV Death



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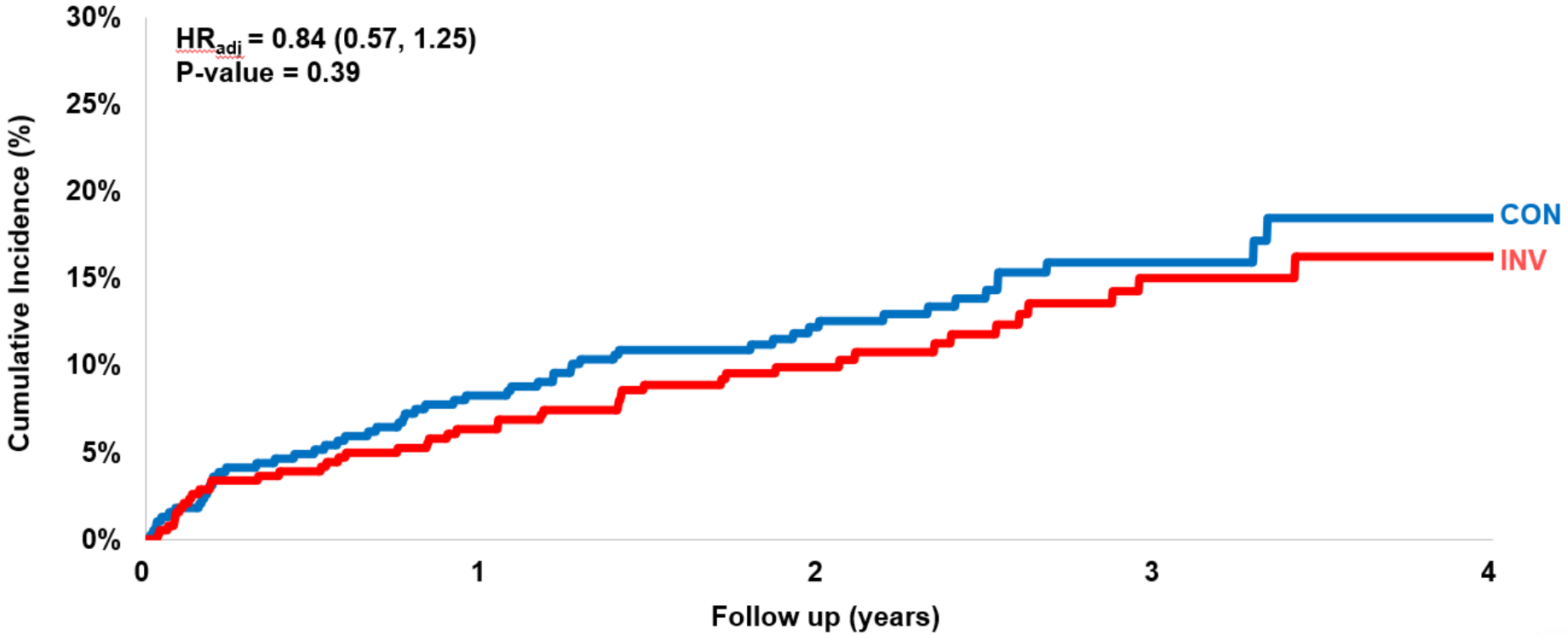
Secondary End Points

Myocardial Infarction



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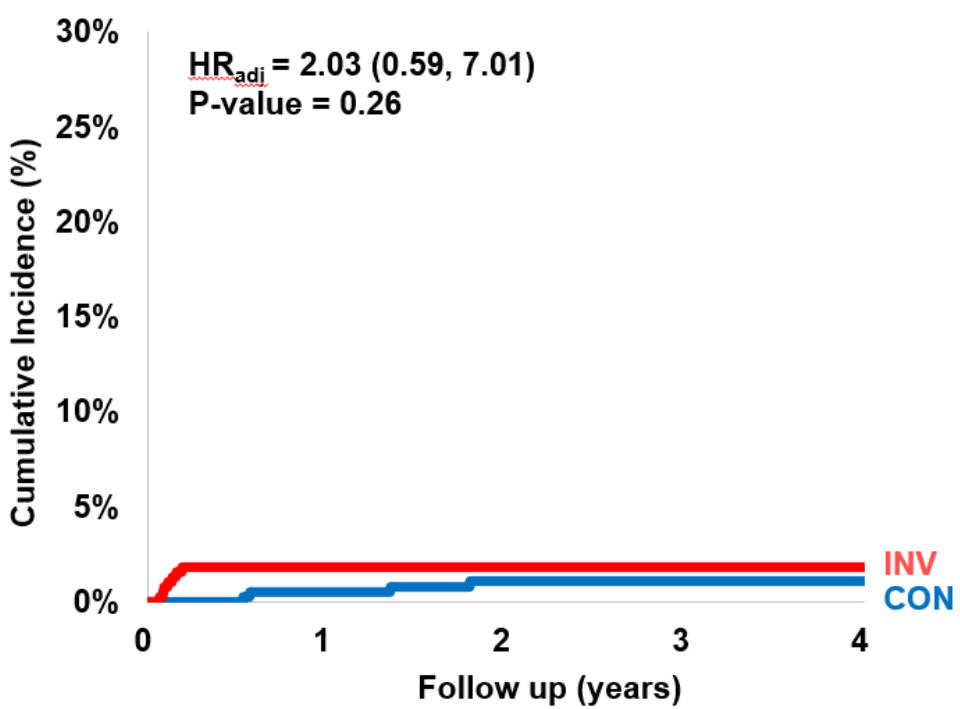
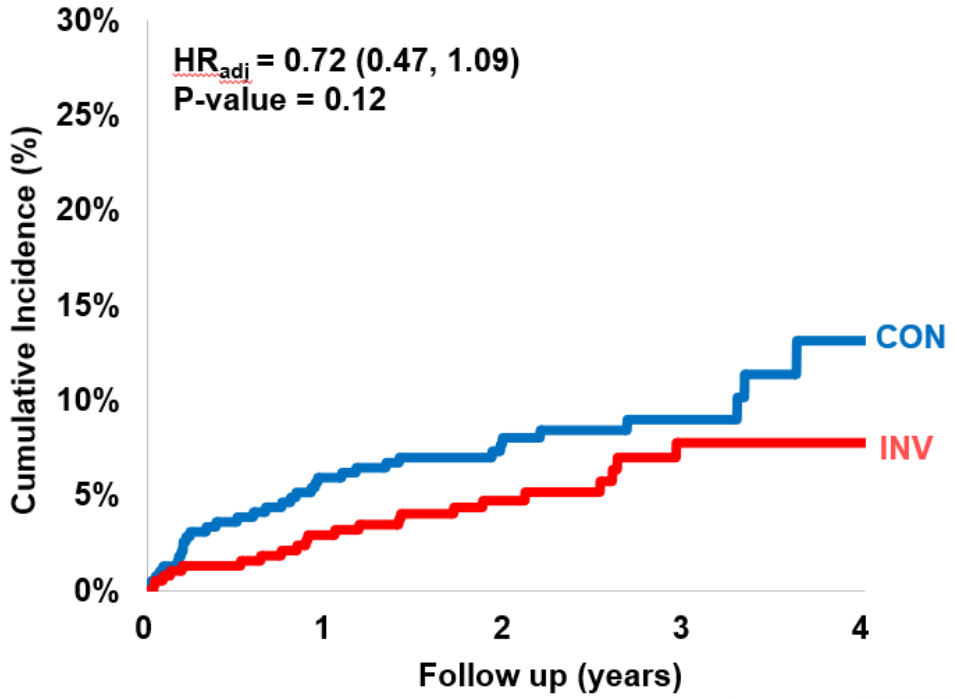
Secondary End Points

Procedural MI



Spontaneous MI



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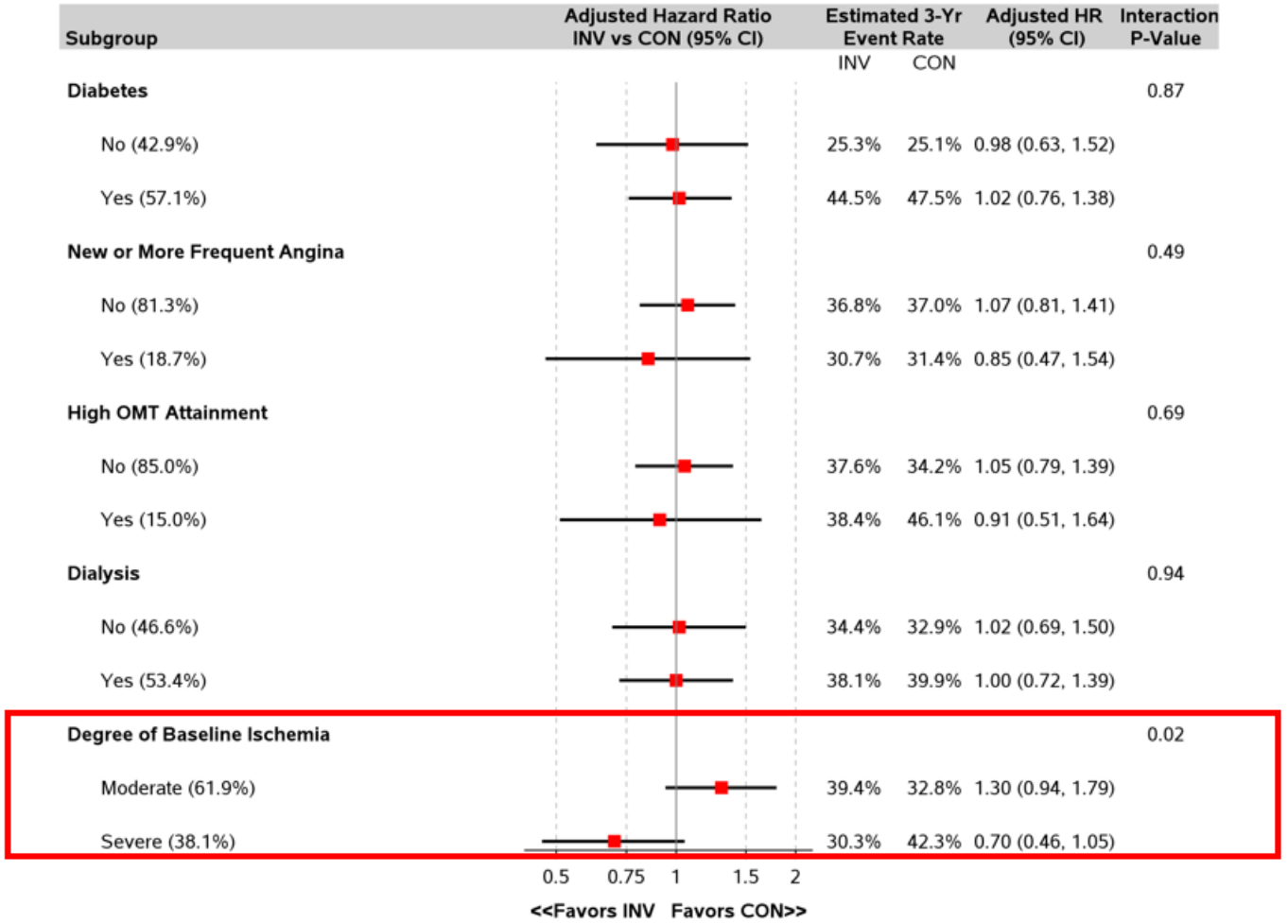
Heterogeneity of Treatment Effect

Death or MI



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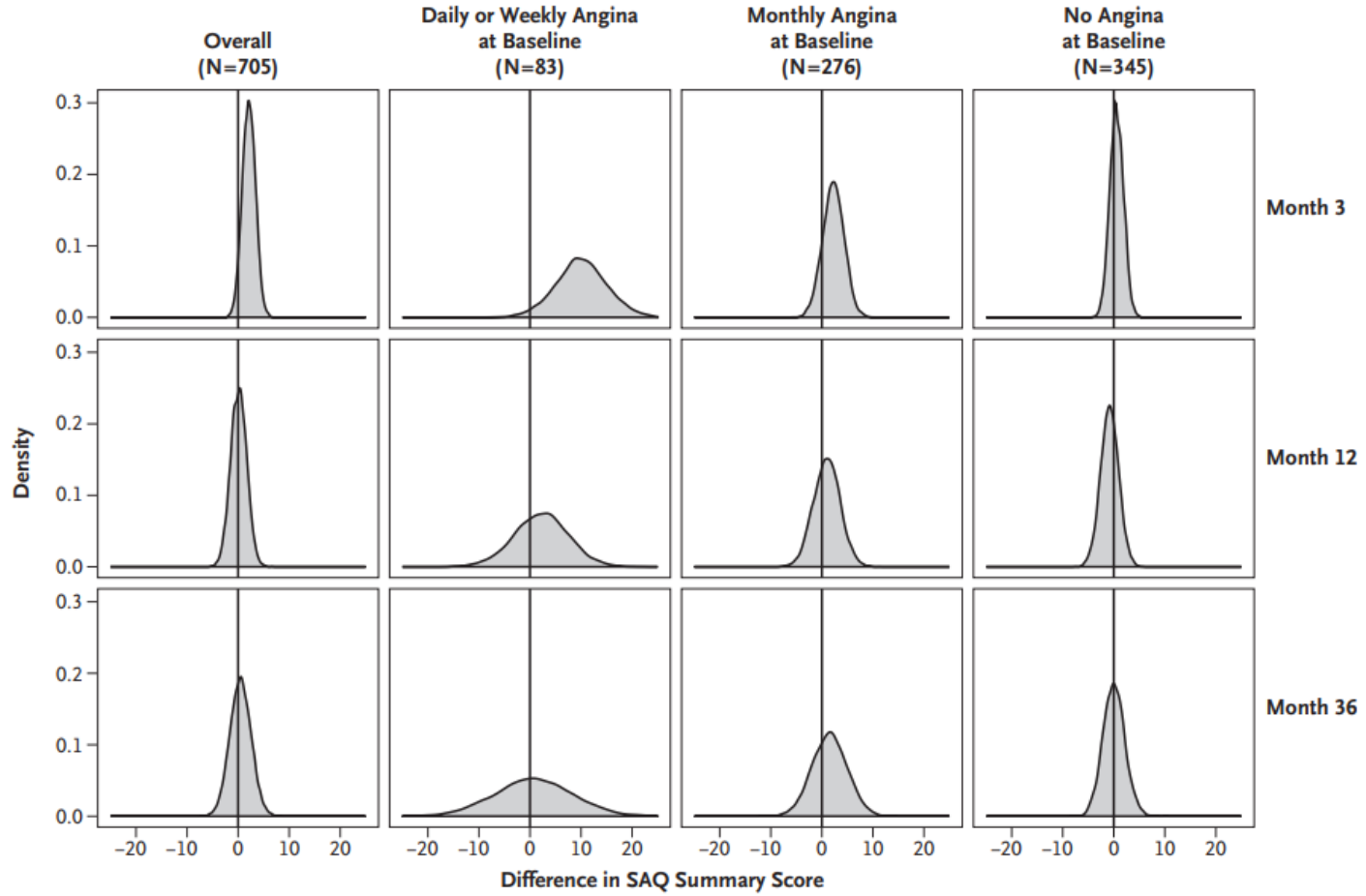

Figure 2. Distributions of Differences between Treatment Groups in SAQ Summary Scores.

Shown are posterior distributions of estimated mean differences between the invasive-strategy group and the conservative-strategy group in the SAQ Summary score, according to angina frequency at baseline (as assessed with the SAQ Angina Frequency score) and time point. Positive numbers on the x axis show the magnitude of benefits with an invasive strategy, and the y axis shows the probability of those benefits.

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Study Limitations

- Low rates of revascularization in the invasive arm
  - Sensitivity and specificity of stress testing in CKD cohort is poor
  - No requirement for CCTA in the trial
- Based on exclusion criteria, the trial results do not apply to patients with:
  - Acute coronary syndromes within 2 months
  - Highly symptomatic patients
  - LVEF <35%

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Conclusions

- Largest trial of invasive vs. conservative strategy in patients with advanced CKD and SIHD
- Low rates of procedural complications (stroke, AKI)
- Overall, an initial invasive strategy did not demonstrate a reduced risk of clinical outcomes as compared with an initial conservative strategy

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Q&A

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