SERVIZO GALEGO de SAÚDE | Complexo Hospitalario Universitario de Santiago de Compostela
Santiago de Compostela

Cardioactualidad 2013.

Cambios con implicaciones clínicas

José R. González Juanatey
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Cardioactualidad 2013

Riesgo Cardiovascular

Cardiopatía Isquémica

Insuficiencia cardíaca

Fibrilación auricular

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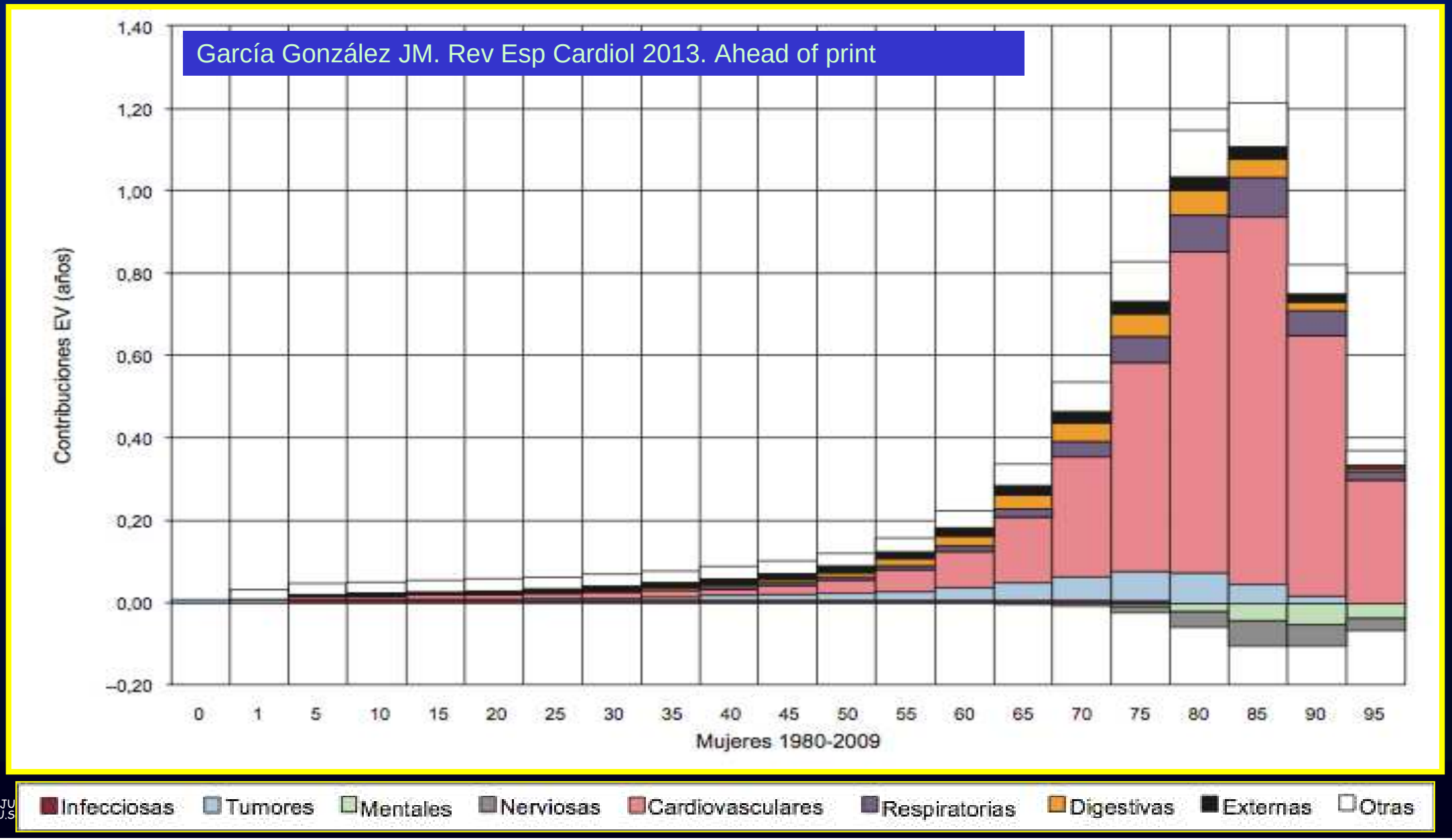
Contribuciones de la mortalidad CV a la esperanza de vida de la población española de 1980 a 2009



Para disminuir el LDL-c
Terapia hipolipemiante

↑ LDL-c → Estatina (hasta la dosis máxima recomendable o tolerada)

- **Inaplicable** → Resina, Niacina, Ezetimiba
- **Intolerada** → Dosis/tipo o/+resina +niacina +ezetimiba
- **Insuficiente**
  - **Obj. LDL-c x** → Dosis/tipo +ezetimiba +resina
  - **noHDL x** → Dosis/tipo +niacina +fibrato?

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Para ↑ HDL-c y ↓ TG

Chapman et al; EAS Consensus Panel, 2011

- **Paciente de alto riesgo**
- **LDL-c en rango**
- **TG > 150 mg/dl y/o**
- **HDL-c < 40 mg/dl**

Intensificar estilo de vida
Buscar causas secundarias
Comprobar cumplimentación

Niacina o fibrato ✗

Intensificar ↓ LDL-c

Dos ensayos clínicos con Fibratos ***(FIELD y ACCORD)*** no han demostrado beneficio en diabéticos y tampoco la Niacina ***(AIM-HIGH y HPS-2)***

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Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

ATP-IV 2013

American Heart Association

Focus on ASCVD Risk Reduction: 4 statin benefit groups

- Based on a comprehensive set of data from RCTs that identified 4 statin benefit groups which focus efforts to reduce ASCVD events in secondary and primary prevention.
- Identifies high-intensity and moderate-intensity statin therapy for use in secondary and primary prevention.

A New Perspective on LDL-C and/or Non-HDL-C Treatment Goals

- The Expert Panel was unable to find RCT evidence to support continued use of specific LDL–C and/or non-HDL–C treatment targets.
- The appropriate intensity of statin therapy should be used to reduce ASCVD risk in *those most likely to benefit.*
- Nonstatin therapies do not provide acceptable ASCVD risk reduction benefits compared to their potential for adverse effects in the routine prevention of ASCVD.

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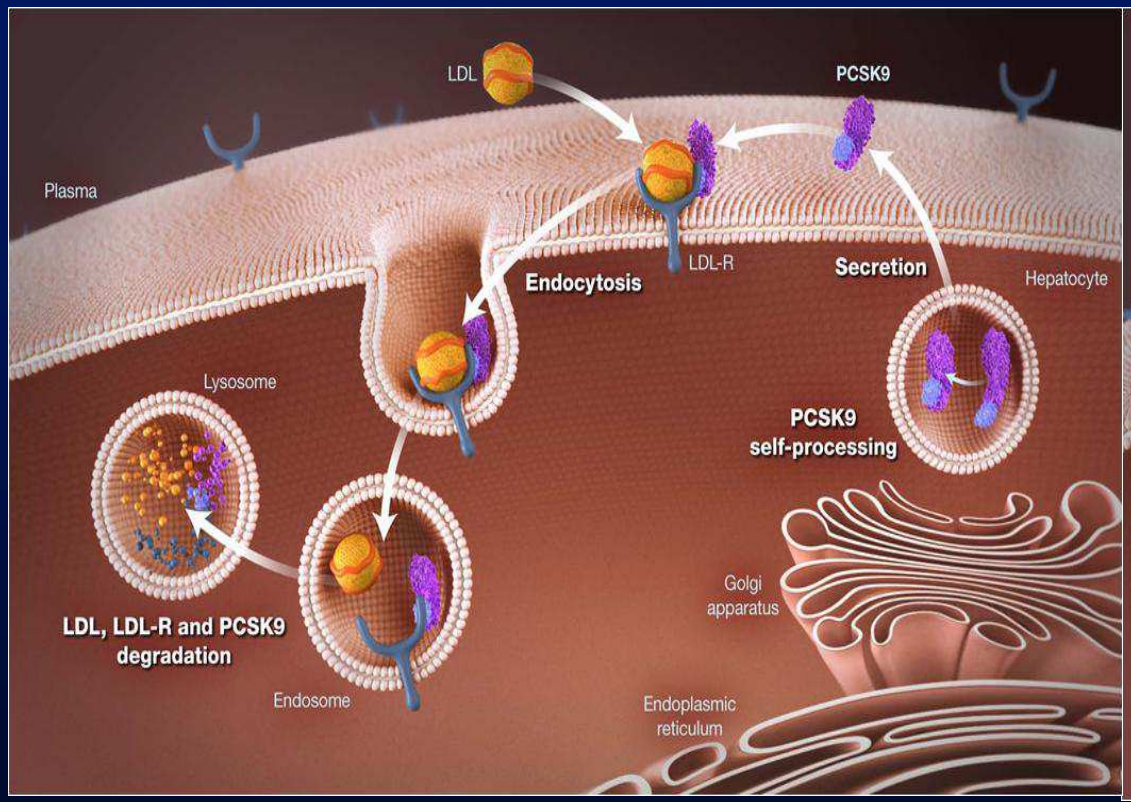
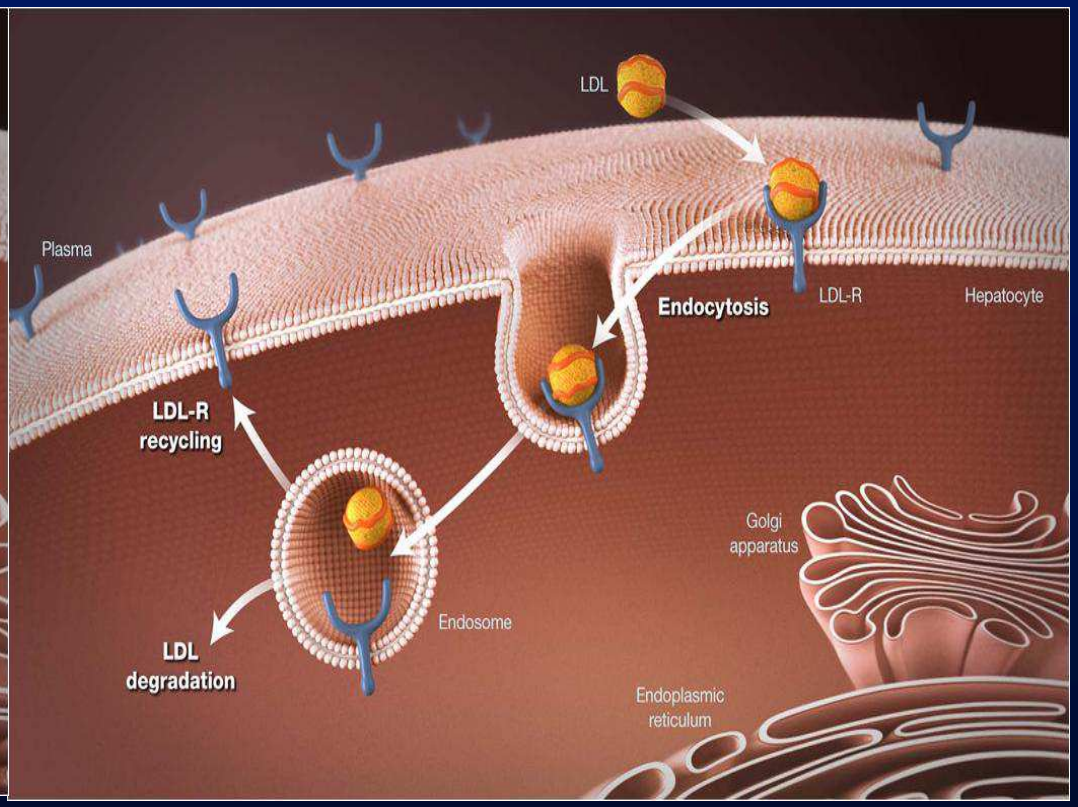
6. ↓ LDL-c: Inhib. Degradación LDL-R

Presencia de PCSK9



- Menos LDL-Receptor
- LDL-C sérico alto

Ausencia de PCSK9



- Más LDL-Receptor
- LDL-C sérico bajo

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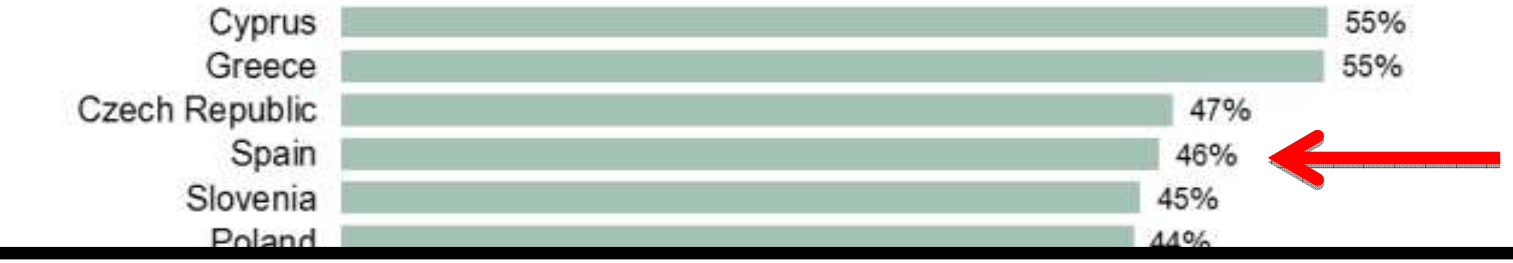
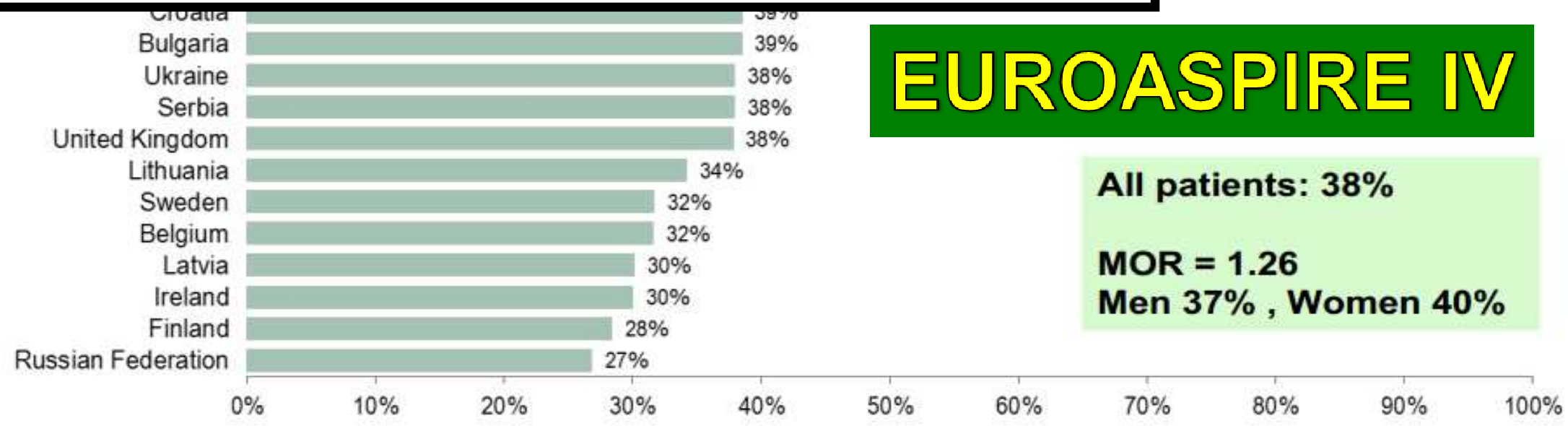
Abifadel M, et al. Nature Genet 2003; 34:154-156

Prevalence of diabetes mellitus*



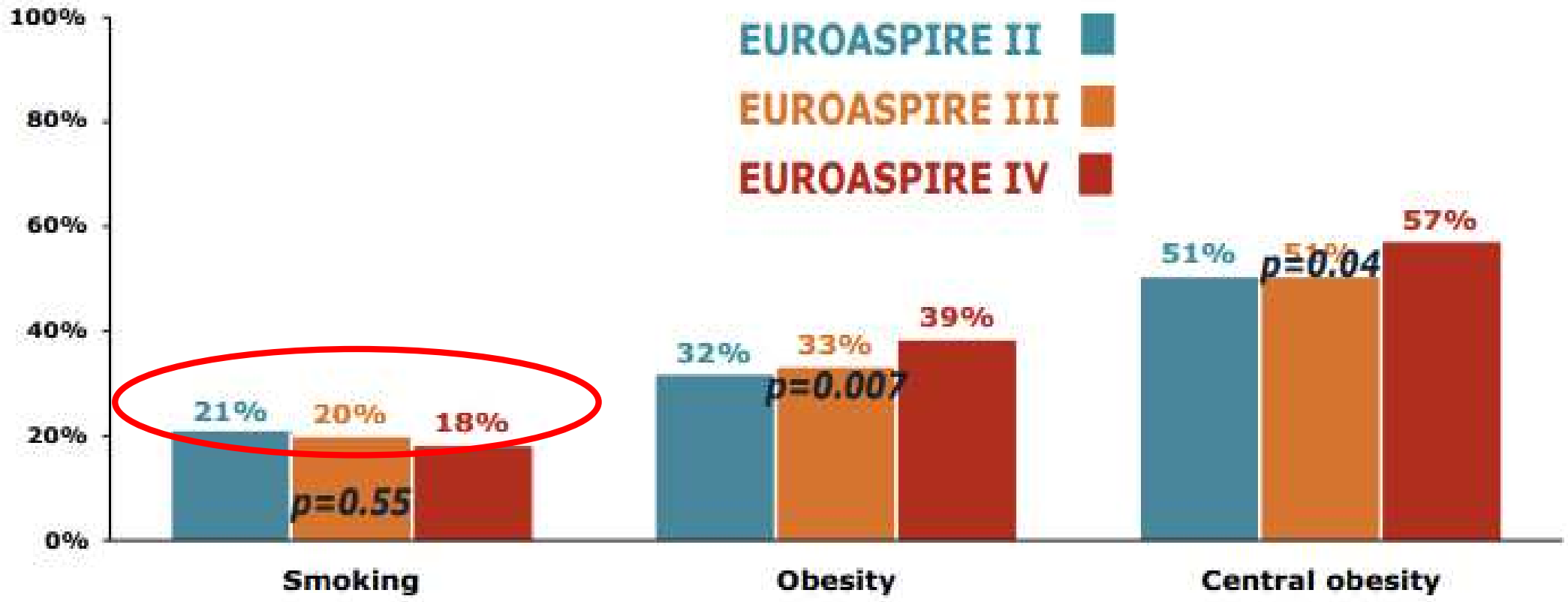
En torno a un 40% de los pacientes son diabéticos



EUROASPIRE IV

All patients: 38%

MOR = 1.26
Men 37% , Women 40%



Peor control de FRCV

* BMI ≥ 30 kg/m²; **Waist circumference ≥ 88 cm for women and ≥ 102 cm for men

Diagnosis of Glucose Perturbations

Se simplifica el diagnóstico

Recommendations	Class	Level
It is recommended that the diagnosis of diabetes is based on HbA_{1c} and FPG combined or on an OGTT if still in doubt.	I	B
It is recommended that an OGTT is used for diagnosing IGT.	I	B
It is recommended that screening for potential T2DM in people with CVD is initiated with HbA_{1c} and FPG and that an OGTT is added if HbA_{1c} and FPG are inconclusive.	I	A

Not – to when needed not perform an Oral Glucose Tolerance Test

Risk Assessment

Estratificación Riesgo Cardiovascular

Recommendations	Class	Level
It should be considered to classify patients with DM as at very high or high risk for CVD depending on the presence of concomitant risk factor and target organ damage.	IIa	B
It is indicated to estimate the urinary albumin excretion rate when performing risk stratification in patients with DM.	I	A
Screening for silent myocardial ischaemia may be considered in selected high risk patients with DM.	IIb	C

Not – to base risk assessment on risk scores

Recommendations	Class	Level
It is not recommended to assess the risk for CVD in patients with DM based on risk scores developed for the general population.	III	B

Manejo Multifactorial DM2

Life style modification

Glycaemic control

HA1C<7%
(individualizar)

Antiplatelet therapy

No en
Prevención 1aria

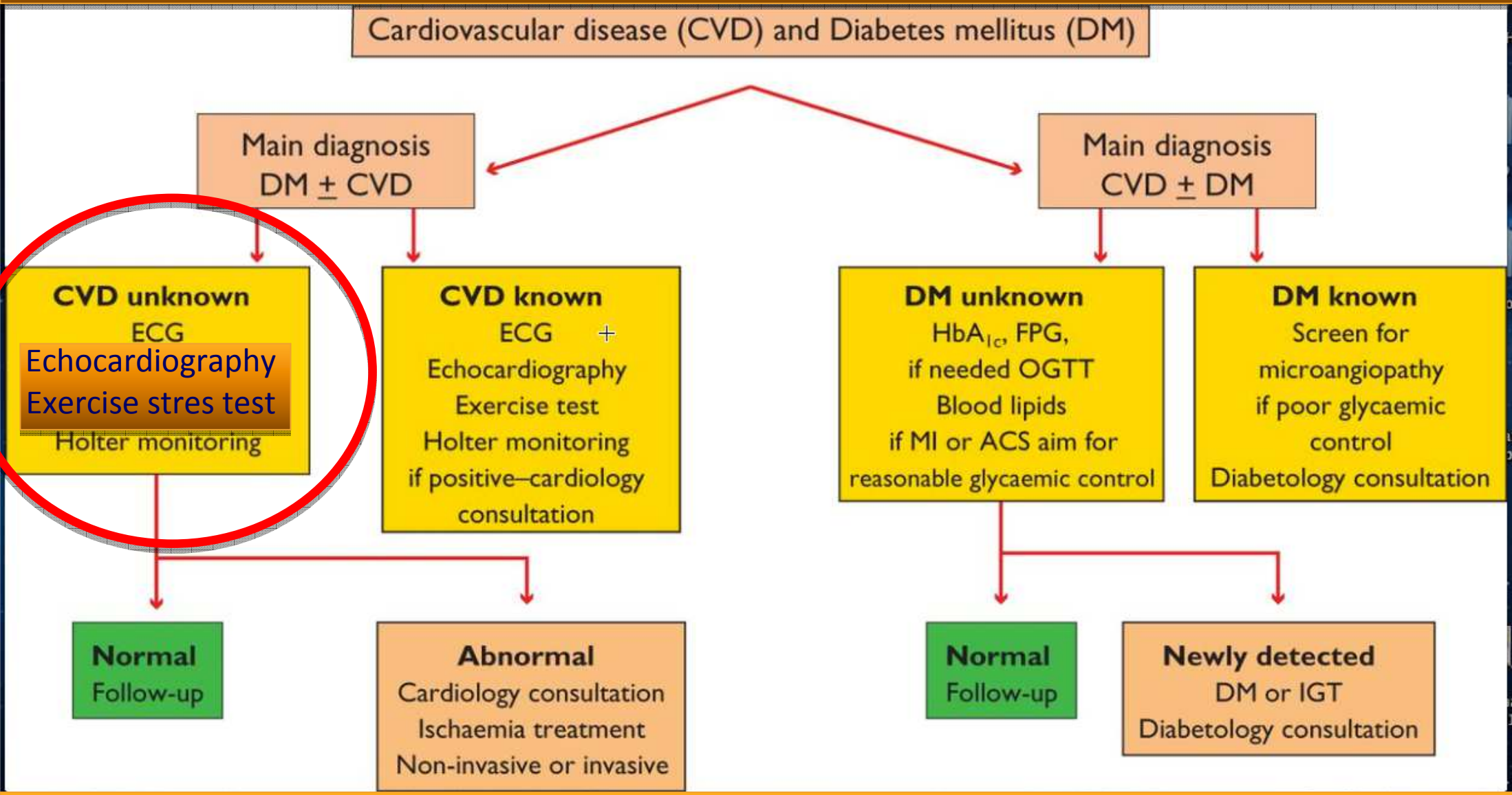
Blood pressure control

<140/85 mm Hg
< 130/85 (Proteinuria)

Lipid control

LDL < 70 mg/dl MAR
< 100 o 50% AR

ESC Diabetes Guidelines 2013



European Heart Journal Advance Access published September 2, 2013

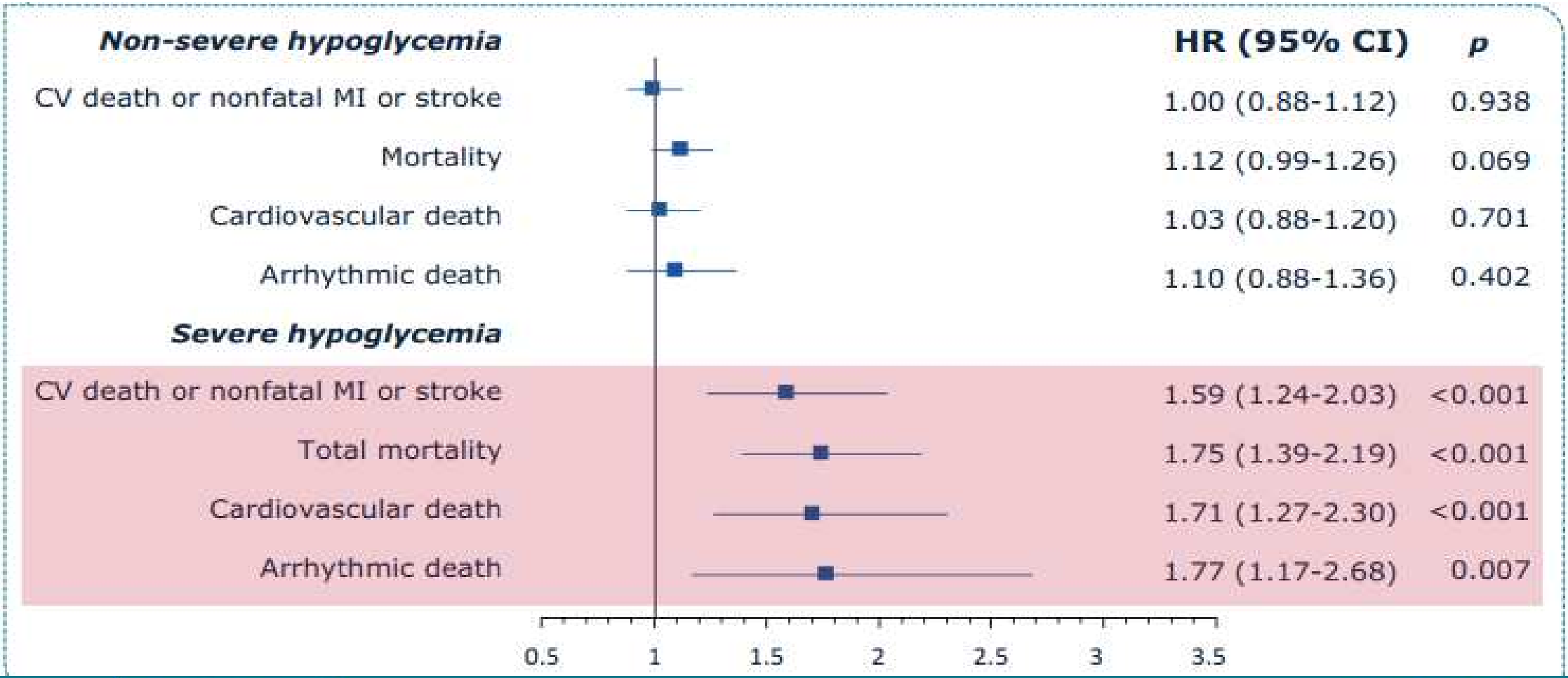
European Heart Journal
doi:10.1093/eurheartj/eht332

FASTTRACK CLINICAL RESEARCH

Disease management

Does hypoglycaemia increase the risk of cardiovascular events? A report from the ORIGIN trial

The ORIGIN Trial Investigators*†



Antidiabetic agents and risk of hypoglycemia

High risk

- Insulin therapy[1]
- Sulphonylureas[2]
- Glinides (less than SUs)[1,3]
- Drug-drug interaction can also potentiate hypoglycaemia[4,5]

Low risk

- Metformin[6]
- a-glucosidase inhibitors[7]
- Thiazolidinediones[6,8]
- GLP-1 agonists[9]
- DPP-4 inhibitors[10-12]

1. Henderson JN, et al. ***Diabet Med.*** 2003;20:1016; 2. Bolen S, et al. ***Ann Intern Med***. 2007;147:386; 3. Kahn SE, et al. ***N Engl J Med***. 2006;355:2427; 4. Krentz AJ, Bailey CJ. *Drugs*. 2005;65:385; 5. Prandin® (repaglinide) package insert. Novo Nordisk; June 2006; 6. Kahn SE, et al. ***N Engl J Med***. 2006;355:2427; 7. Cefalu WT. ***Nature***. 2007;81:636; 8. Bolen S, et al. ***Ann Intern Med***. 2007;147:386; 9. DeFronzo RA, et al. ***Diabetes Care.*** 2005;28:1092; 10. Stonehouse A. ***Curr Diabetes Rev*** 2008;4:101; 11. Aschner P et al. ***Diabetes Care.*** 2006; 29:2632; 12. Rosenstock J et al. ***Diabetes Obes Metab*** 2008;10:376.

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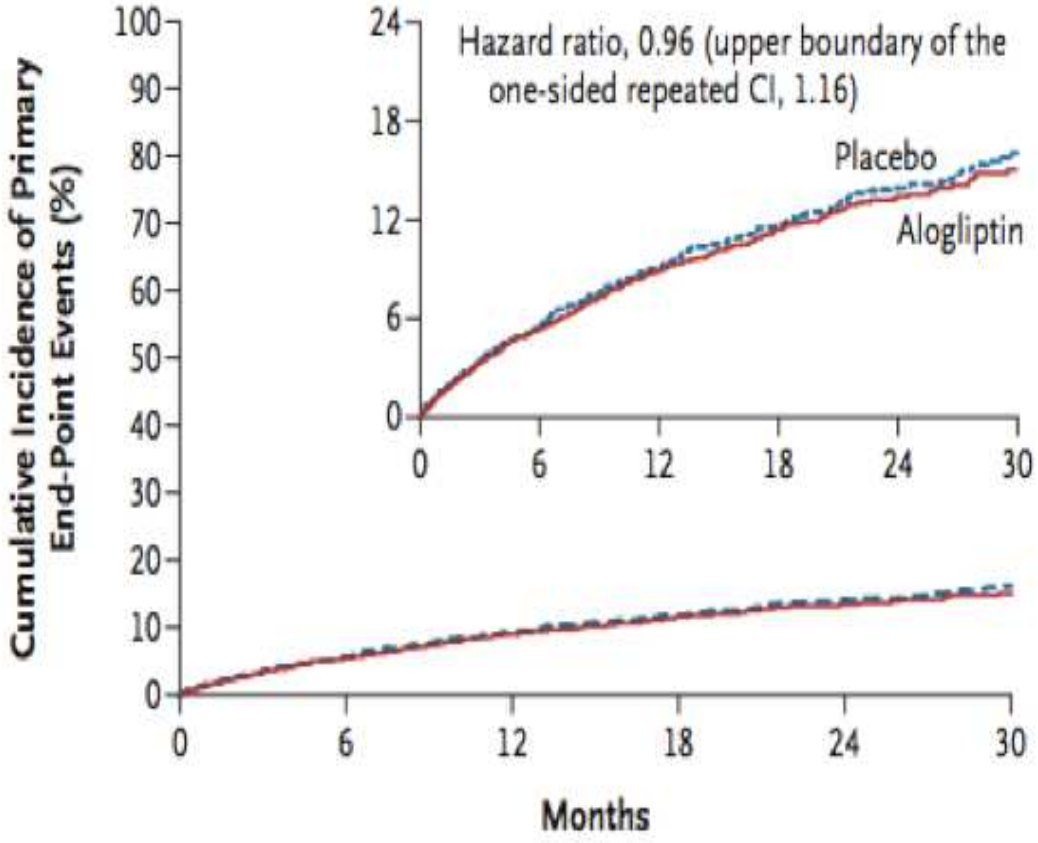
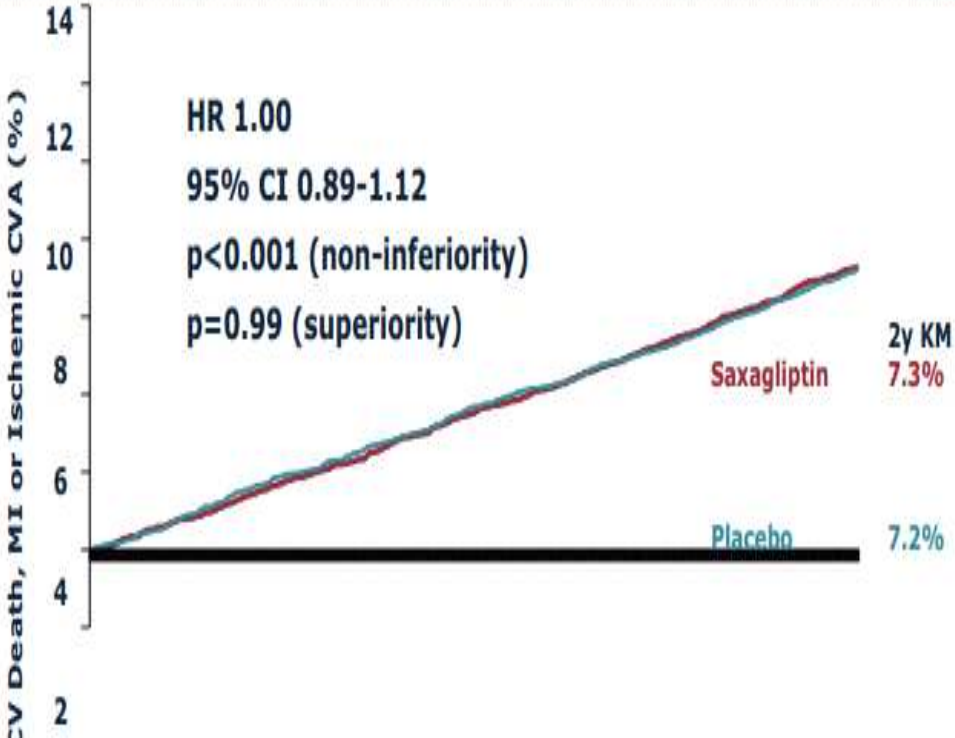
EXAMINE

savor TIMI 53

TIMI STUDY GROUP / HADASSAH MEDICAL ORG



No. at Risk						
Placebo	2679	2299	1891	1375	805	286
Alogliptin	2701	2316	1899	1394	821	296



Placebo	8212	7983	7761	7267	4855
Saxagliptin	8280	8071	7836	7313	4920

IDPP4 and HF Risk in Diabetics

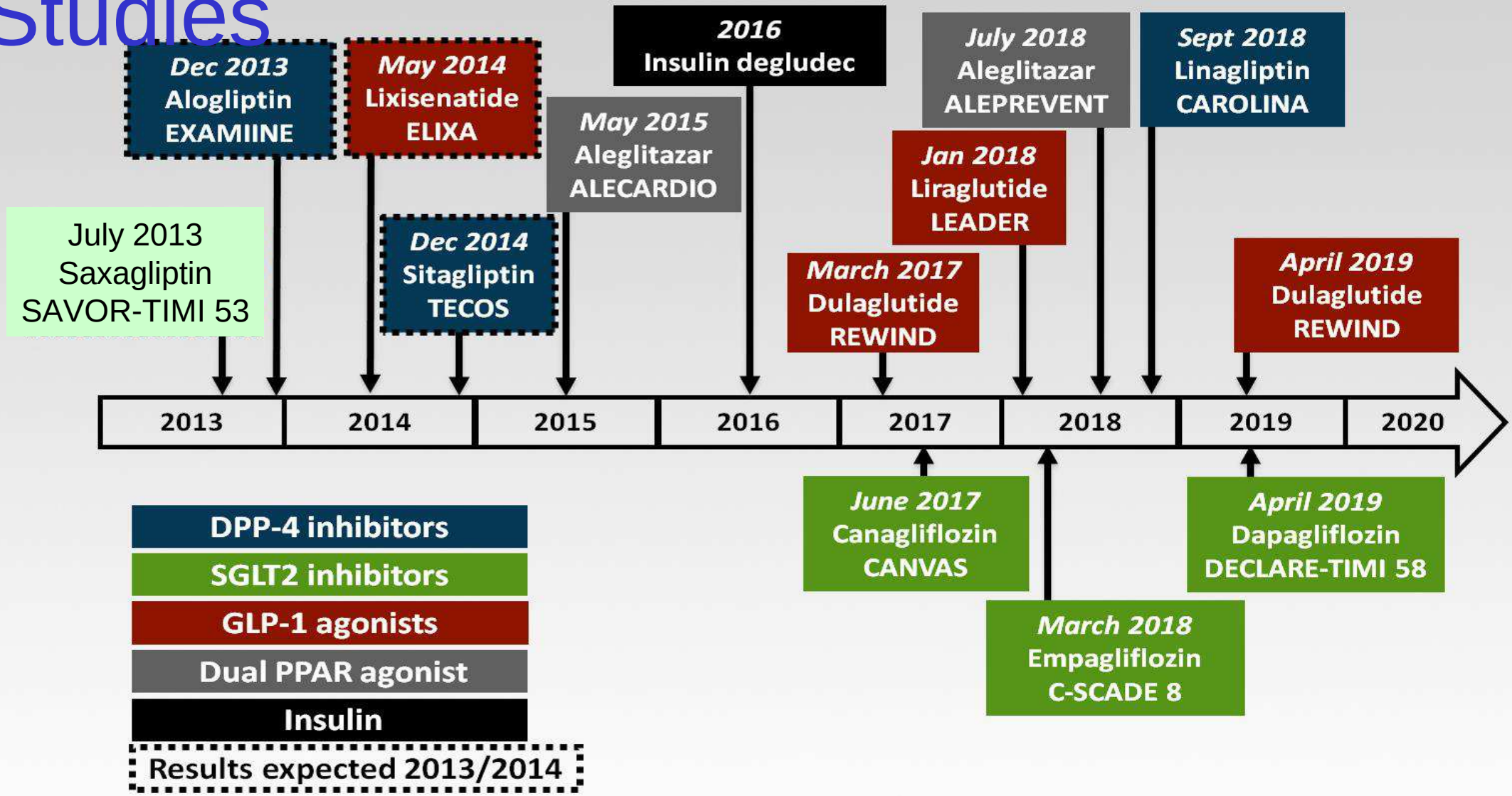
savor TIMI 53

2-year KM rate (%)

	Placebo (N=8,212)	Saxagliptin (N=8,280)	HR	*p value for superiority*
CV Death	2.9	3.2	1.03 (0.87-1.22)	0.72
MI	3.4	3.2	0.95 (0.80-1.12)	0.52
Ischemic Stroke	1.7	1.9	1.11 (0.88-1.39)	0.38
Hosp for Cor. Revasc	5.6	5.2	0.91 (0.80-1.04)	0.18
Hosp for UA	1.0	1.2	1.19 (0.89-1.60)	0.24
Hosp for Heart Failure	2.8	3.5	1.27 (1.07-1.51)	0.007
All-Cause Mortality	4.2	4.9	1.11 (0.96-1.27)	0.15

N Engl J Med 2013

Timelines for Ongoing Outcomes Studies



Cardioactualidad 2013

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Fibrilación auricular

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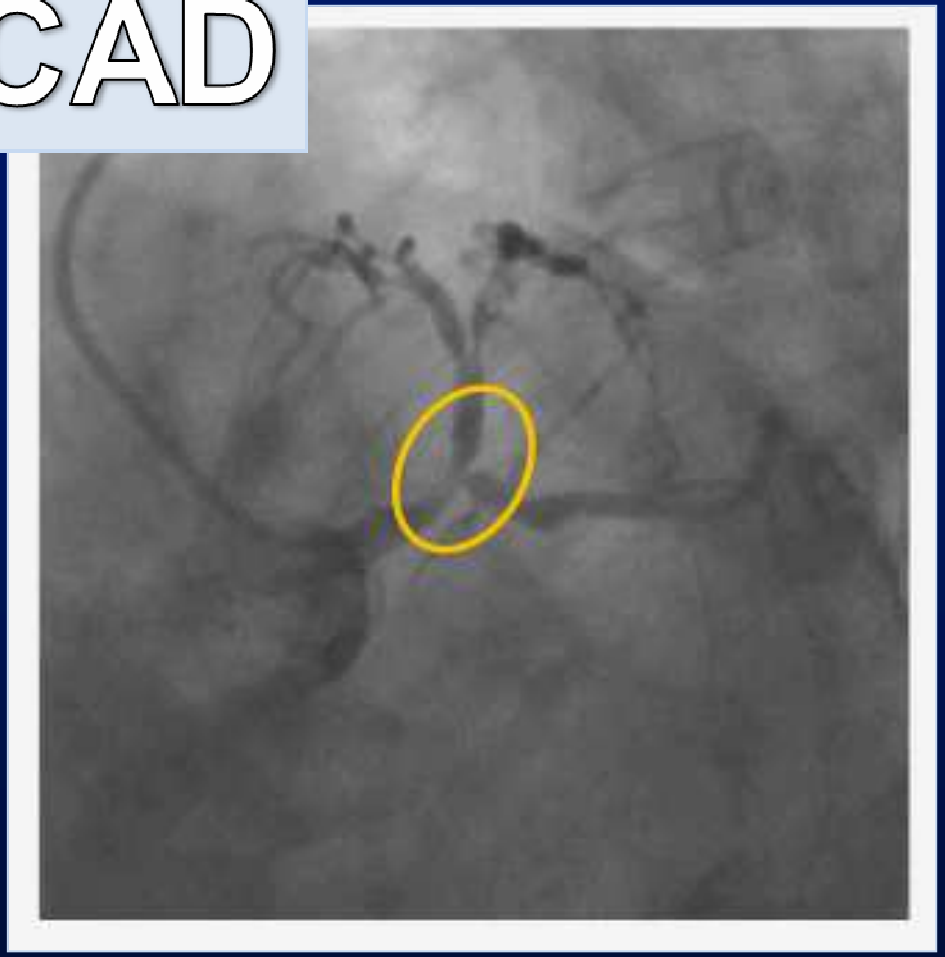
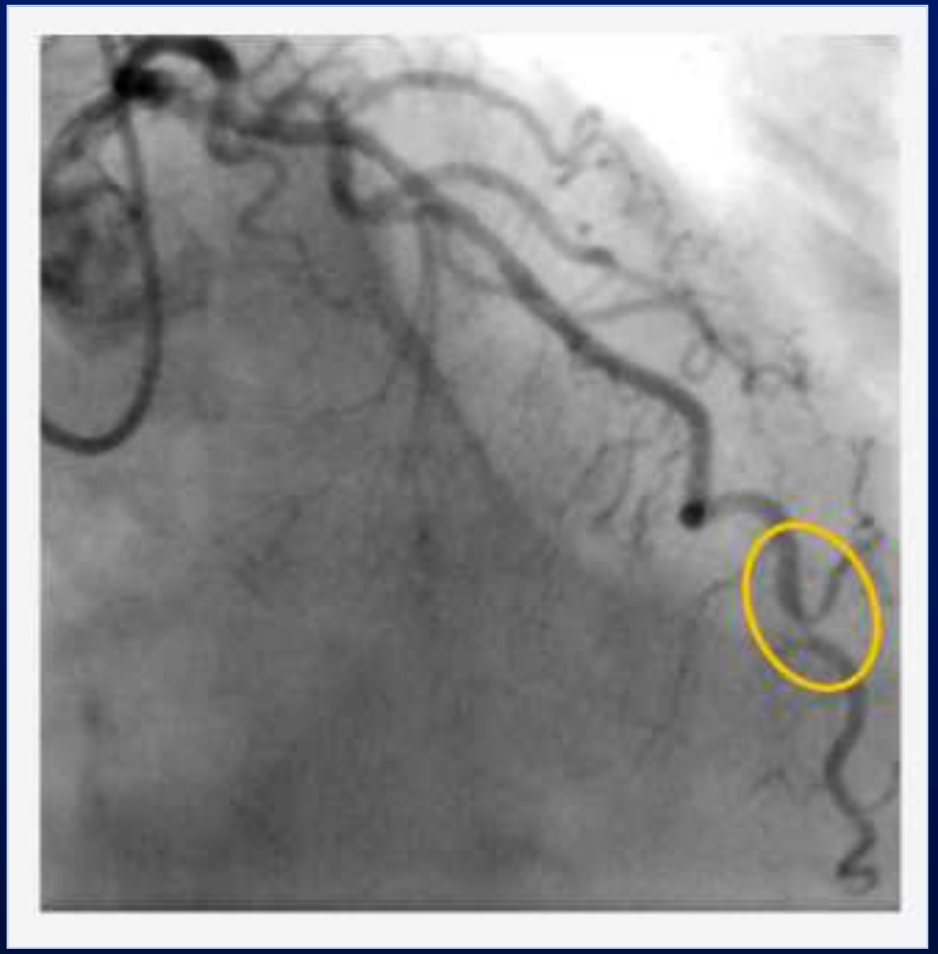
SCAD





All patients with SCAD require medical therapy (ASA, statins, Anti-anginal)

Not All patients with coronary artery stenoses benefit from revascularization

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Clinical Likelihood of Disease

Typical angina (definite)	Meets all three of the following characteristics: • substernal chest discomfort of characteristic quality and duration; • provoked by exertion or emotional stress; • relieved by rest and/or nitrates within minutes.
Atypical angina (probable)	Meets two of these characteristics.
Non-anginal chest pain	Lacks or meets only one or none of the characteristics.

2013 ESC guidelines on the management of stable coronary artery disease

The Task Force on the management of stable coronary artery disease of the European Society of Cardiology

	Typical angina		Atypical angina		Non-anginal pain	
Age	Men	Women	Men	Women	Men	Women
30–39	59	28	29	10	18	5
40–49	69	37	38	14	25	8
50–59	77	47	49	20	34	12
60–69	84	58	59	28	44	17
70–79	89	68	69	37	54	24
>80	93	76	78	47	65	32

Thomas Cuisset (France), Car… (France), Nikolaus Marx (Germ… Manel Sabaté (Spain), Roxy S…

ESC Committee for Practice … (Germany), Jeroen J. Bax (Ne… (Belgium), Roberto Ferrari (Ita… Philippe Kolh, (Belgium), Patri… Piotr Ponikowski (Poland), Per… (Belgium), Stephan Windecker…

Document Reviewers: Juhan… Marc J. Claeys (Belgium), Nor… Oliver Gaemperli (Switzerland)… Stefan K. James (Sweden), Ka… Aldo Pietro Maggioni (Italy), M… (Netherlands), Per Anton Sirne… Aylin Yildirir (Turkey), Jose Luis Zamorano (Spain).

…many), Jean-Sebastien Hulot …k), Frank Ruschitzka (Switzerland), …rints (Belgium).

…nany), Helmut Baumgartner … (Turkey), Robert Fagard …ani Knuuti (Finland), …ssimo F. Piepoli (Italy), …cki (Poland),William Wijns

…), Héctor Bueno (Spain), …nck-Brentano (France), …een Husted (Denmark), … Lancellotti (Belgium), …weden), Maarten L. Simoons …an Windecker (Switzerland),

This risk is modified if

- ECG indicates abnormalities
- LV EF < 50%

Bajo riesgo: menos 15%

Intermedio riesgo: 15-65%

Alto riesgo: 66-85%

Muy alto riesgo: más 85%

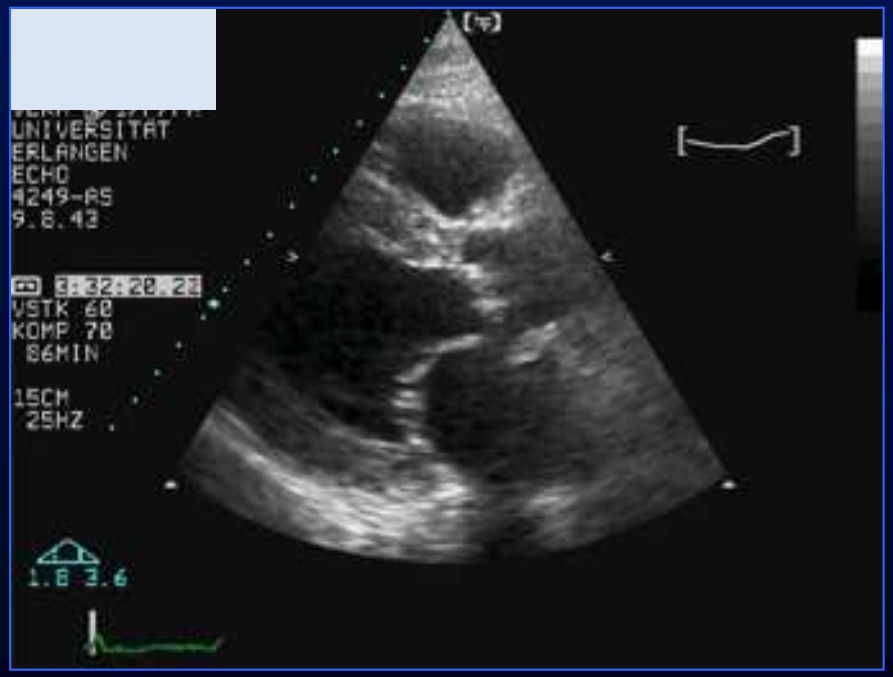
EUROPEAN SOCIETY OF CARDIOLOGY®

Basic Diagnostic Testing

ECG

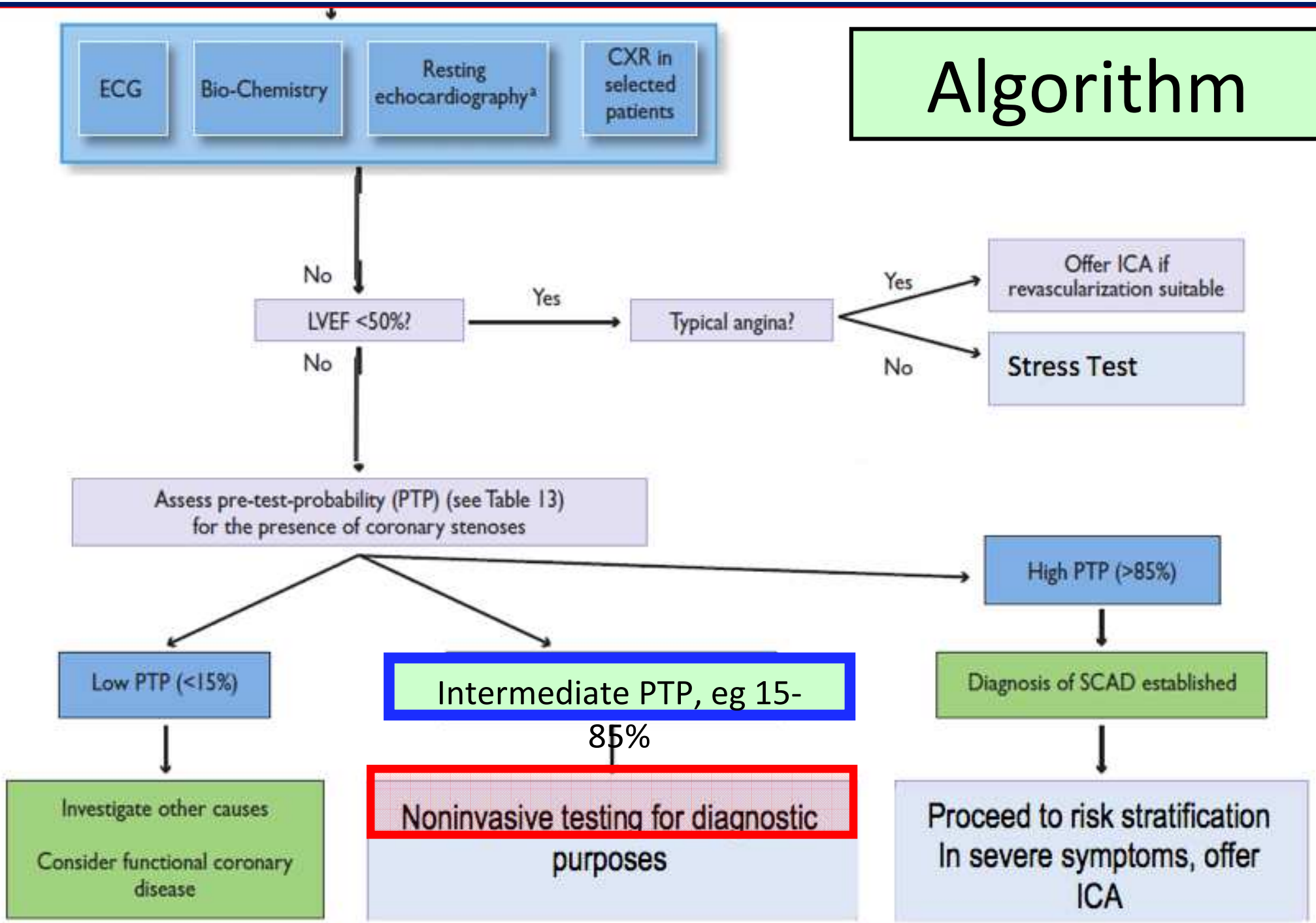
Recommendations	Class [a]	Level [b]	Ref. [c]
A resting ECG is recommended in all patients at presentation.	I	C	-

Echo

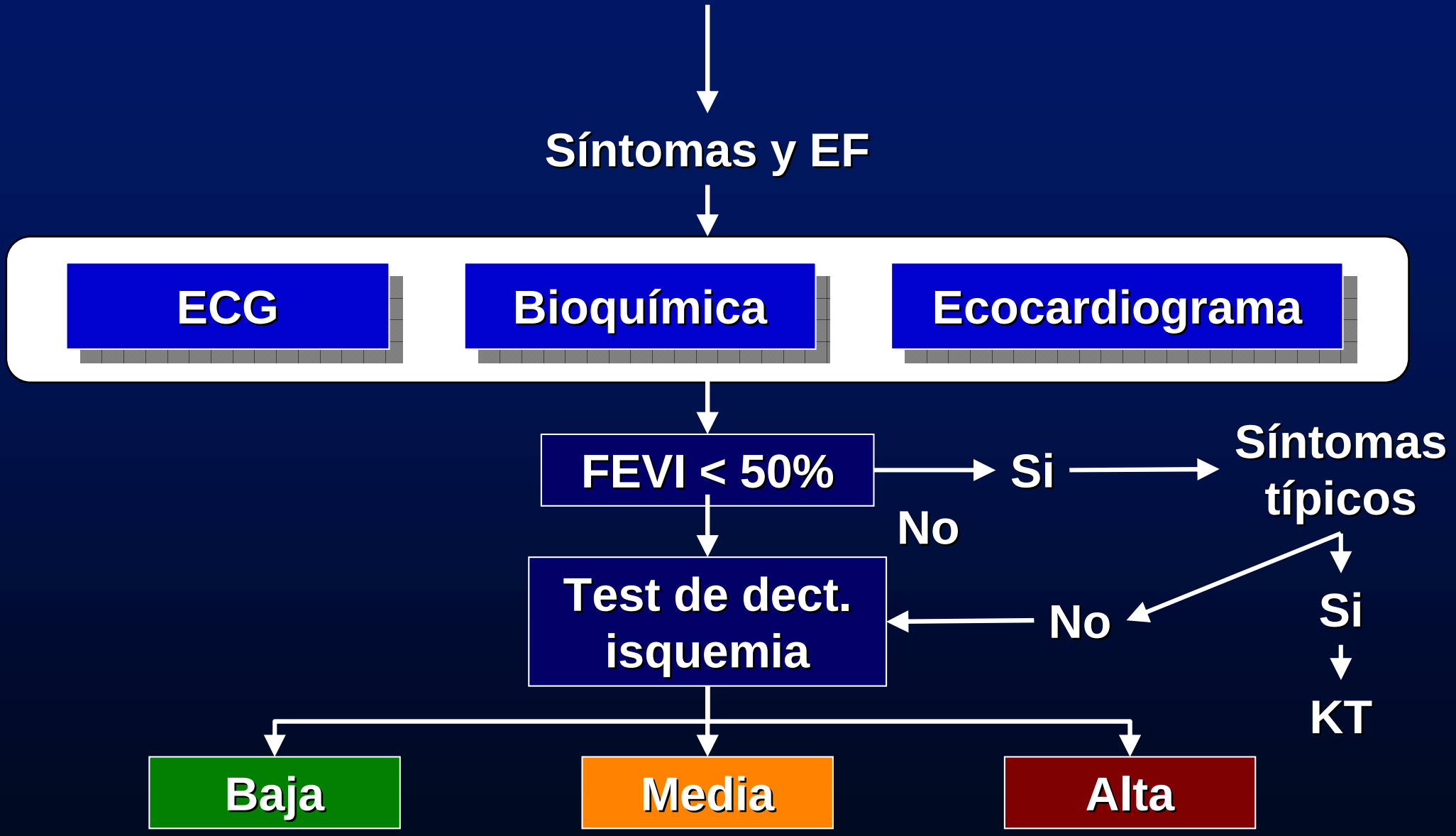


Recommendations	Class [a]	Level [b]	Ref. [c]
A resting transthoracic echocardiogram is recommended in all patients for: a) exclusion of alternative causes of angina; b) identification of regional wall motion abnormalities suggestive of CAD; c) measurement of LVEF for risk stratification purpose; d) evaluation of diastolic function.	I	B	27, 79, 80

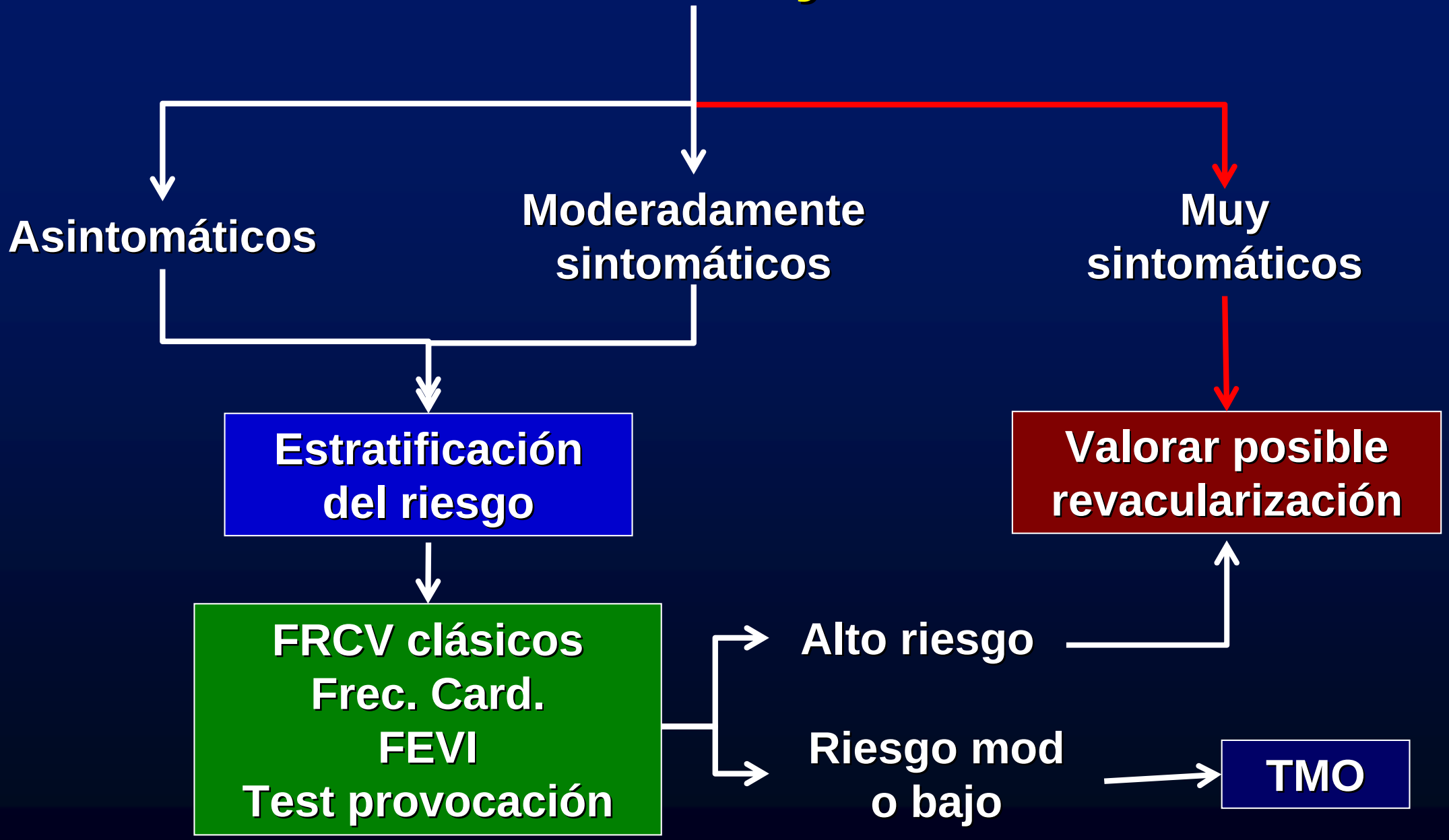
Algorithm


ECG
Bio-Chemistry
Resting echocardiography[a]
CXR in selected patients
No
LVEF <50%?
Yes
Typical angina?
Yes
Offer ICA if revascularization suitable
No
Stress Test
No
Assess pre-test-probability (PTP) (see Table 13) for the presence of coronary stenoses
High PTP (>85%)
Low PTP (<15%)
Intermediate PTP, eg 15-85%
Diagnosis of SCAD established
Investigate other causes
Consider functional coronary disease
Noninvasive testing for diagnostic purposes
Proceed to risk stratification
In severe symptoms, offer ICA

Pacientes primera evaluación

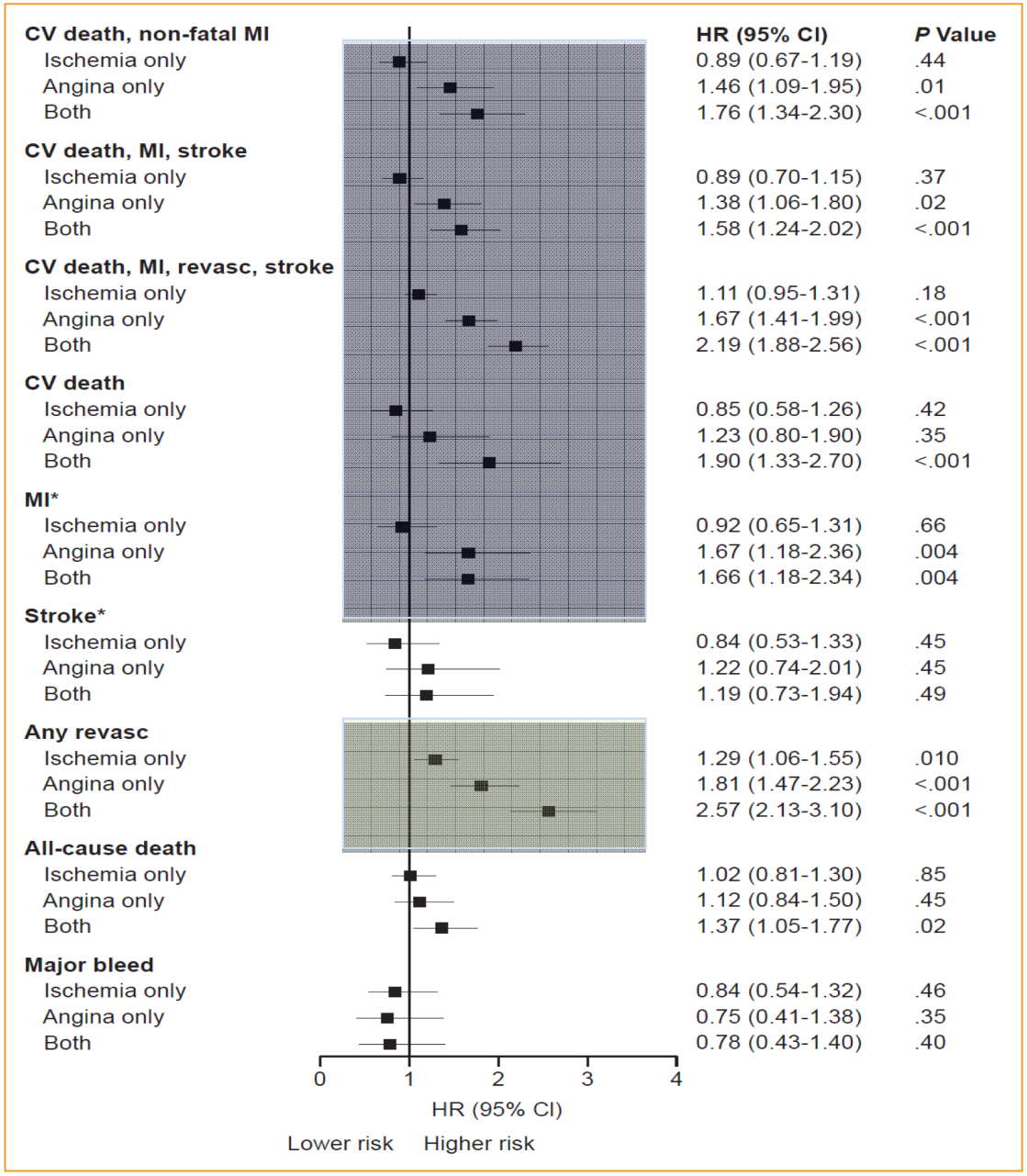


Pacientes con AE y CI crónica



Prevalence of Anginal Symptoms and Myocardial Ischemia and their Impact on Clinical Outcomes in Stable Outpatients with Coronary Artery Disease

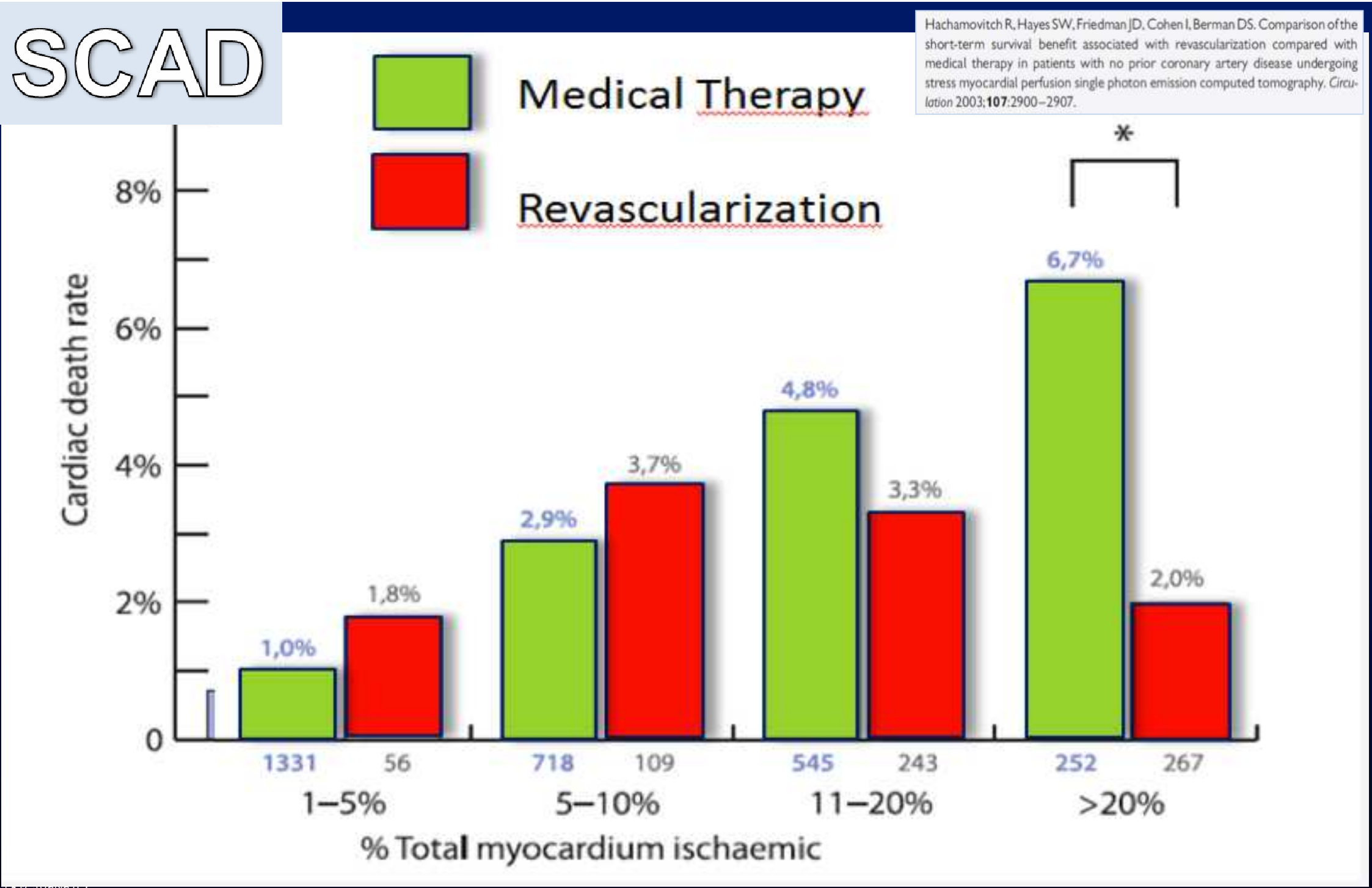
Adjusted HRs for the Primary and Various Composite Outcomes, for Patients with Ischemia, Angina, and Both, Relative to Patients With Neither



Presented at ESC 2013

SCAD

Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. *Circulation* 2003;**107**:2900–2907.



2013 ESC guidelines on the management of stable coronary artery disease

Angina relief

1st line

Short-acting Nitrates, *plus*

BB or CCB-heart rate –
Consider CCB-DHP if low HR or int/contrai.
Consider BB+CCB-DHP if CCSAngina>2

May add or switch (1st line for some cases)

2nd line

Ivabradine HR > 60 bpm
Long-acting nitrates
Nicorandil
Ranolazine
Trimetazidine

Event Prevention

Lifestyle management
Control of risk factors

+ Educate the patient

Aspirine
Statins
Consider ACEI or ARBs

+ Consider Angio, PCI or CABG

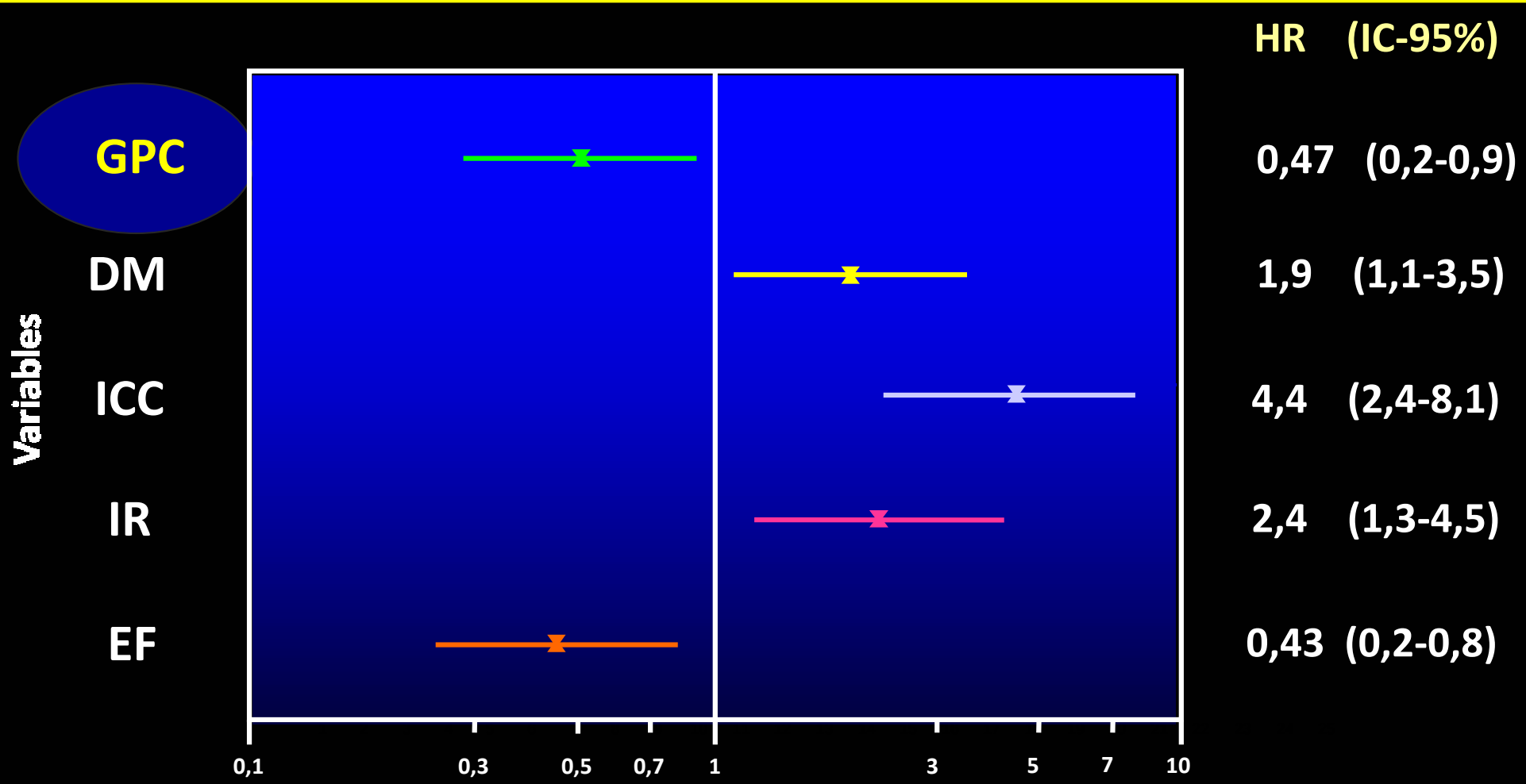
Contents lists available at SciVerse ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Determinants of cardiovascular mortality in a cohort of primary care patients with chronic ischemic heart disease. BARBANZA Ischemic Heart Disease (BARIHD) study

Rafael Vidal-Perez [a,*], Fernando Otero-Raviña [b], Manuel Franco [c], José M. Rodríguez Garcia [d], Rosa Liñares Stolle [e], Ramona Esteban Álvarez [f], Cristina Iglesias Díaz [g], Elena Outeiriño López [h], María José Vázquez López [f], José Ramón Gonzalez-Juanatey [a] and on behalf of the BARBANZA investigators



GPC: Cumplimiento recomendaciones Guías de Práctica Clínica; DM: diabetes; ICC: insuficiencia cardíaca; IR: insuficiencia renal; EF: ejercicio físico

Cardioactualidad 2013

Riesgo Cardiovascular

Cardiopatía Isquémica

Insuficiencia cardíaca

Fibrilación auricular

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C.H.U.Santiago

2013 ACCF/AHA GUIDELINE FOR THE MANAGEMENT OF HEART FAILURE

Clinical events and findings useful for identifying patients with advance HF

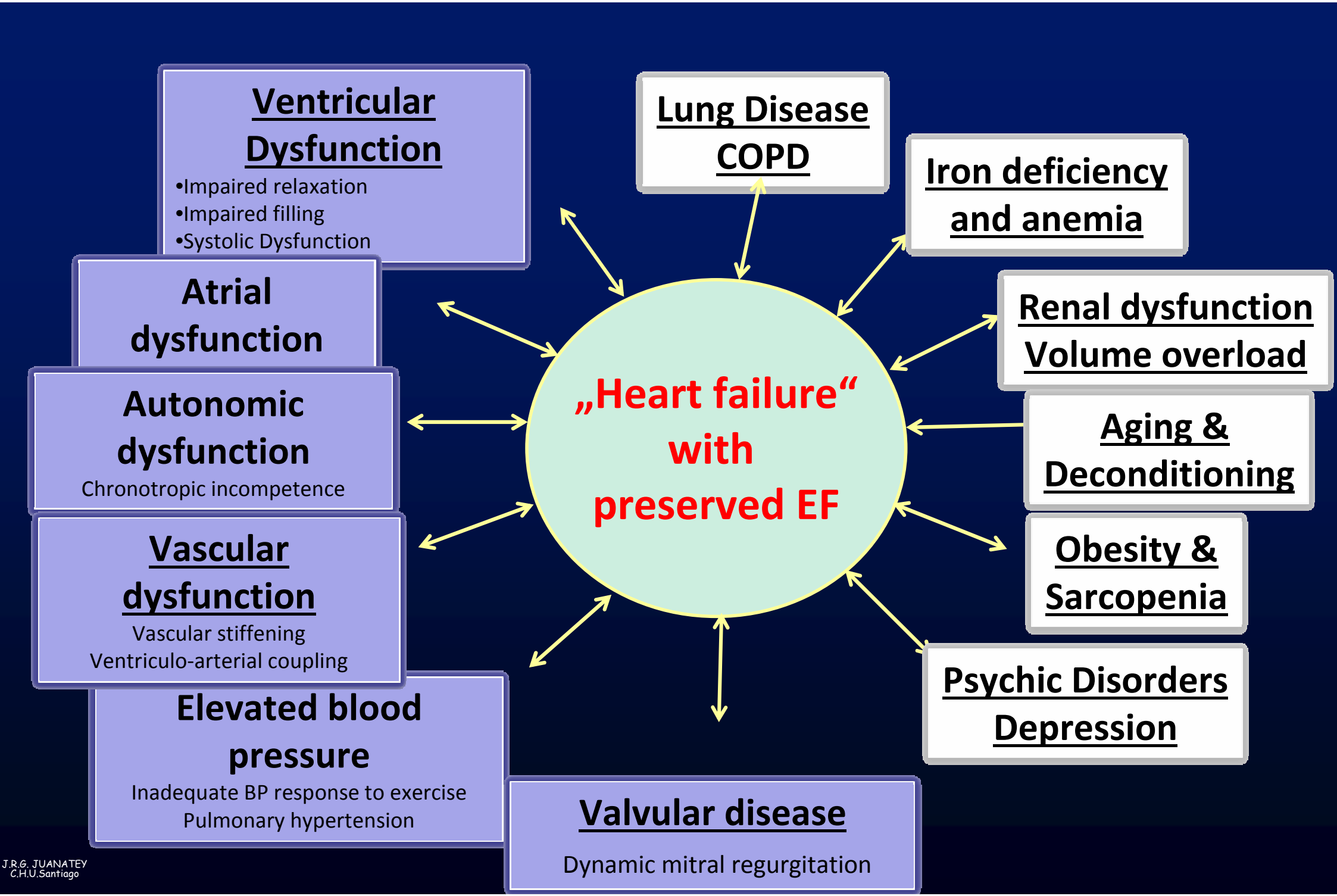
Repeated (>2) hospitalizations or ED visits for HF in the past year
Progressive deterioration in renal function
Weight loss without other cause (e.g. Cardiac cachexia) Progressive decline in serum sodium, usually to <133 mEq/L
Intolerance to ACE inhibitors due to hipoTA and/or worsening renal function
Intolerance to beta blockers due to horsening HF or hypotension
Frequent SBP <90 mmHg Frequent ICD shocks
Persistent dyspnea with dressing or bathing requiring rest Inability to walk 1 block on the level ground due to dyspnea or fatigue
Recent need to escalate diuretics to maintain volume status, daily furosemide >160 mg and/or use of metolazone therapy

Recommendation	COR	LOE	References
Diuretics			
Diuretics are recommended in patients with HF*r*EF with fluid retention	I	C	N/A
ACE inhibitors			
ACE inhibitors are recommended for all patients with HF*r*EF	I	A	(343, 412-414)
ARBs			
ARBs are recommended in patients with HF*r*EF who are ACE inhibitor intolerant	I	A	(108, 345, 415, 450)
ARBs are reasonable as alternatives to ACE inhibitors as first-line therapy in HF*r*EF	IIa	A	(451-456)
Addition of an ARB may be considered in persistently symptomatic patients with HF*r*EF on GDMT	IIb	A	(420, 457)
Routine *combined* use of an ACE inhibitor, ARB, and aldosterone antagonist is potentially harmful	III: Harm	C	N/A
Beta blockers			
Use of 1 of the 3 beta blockers proven to reduce mortality is recommended for all stable patients	I	A	(346, 416-419, 448)
Aldosterone receptor antagonists			
Aldosterone receptor antagonists are recommended in patients	I	A	(425, 426,

2013 ACCF / AHA HF STAGE C *HFrEF*

HFPEF, HFNEF, or Diastolic Heart Failure??

The Relationship Between Pressure and Volume


Ventricular Dysfunction
•Impaired relaxation
•Impaired filling
•Systolic Dysfunction
Lung Disease COPD
Iron deficiency and anemia
Atrial dysfunction
Renal dysfunction Volume overload
Autonomic dysfunction
Chronotropic incompetence
„Heart failure“ with preserved EF
Aging & Deconditioning
Vascular dysfunction
Vascular stiffening
Ventriculo-arterial coupling
Obesity & Sarcopenia
Psychic Disorders Depression
Elevated blood pressure
Inadequate BP response to exercise
Pulmonary hypertension
Valvular disease
Dynamic mitral regurgitation
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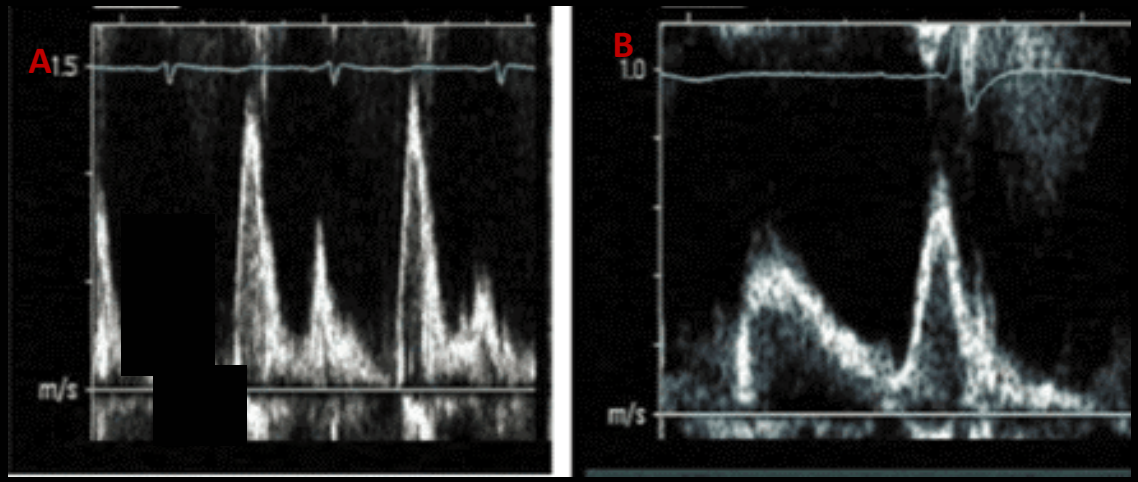
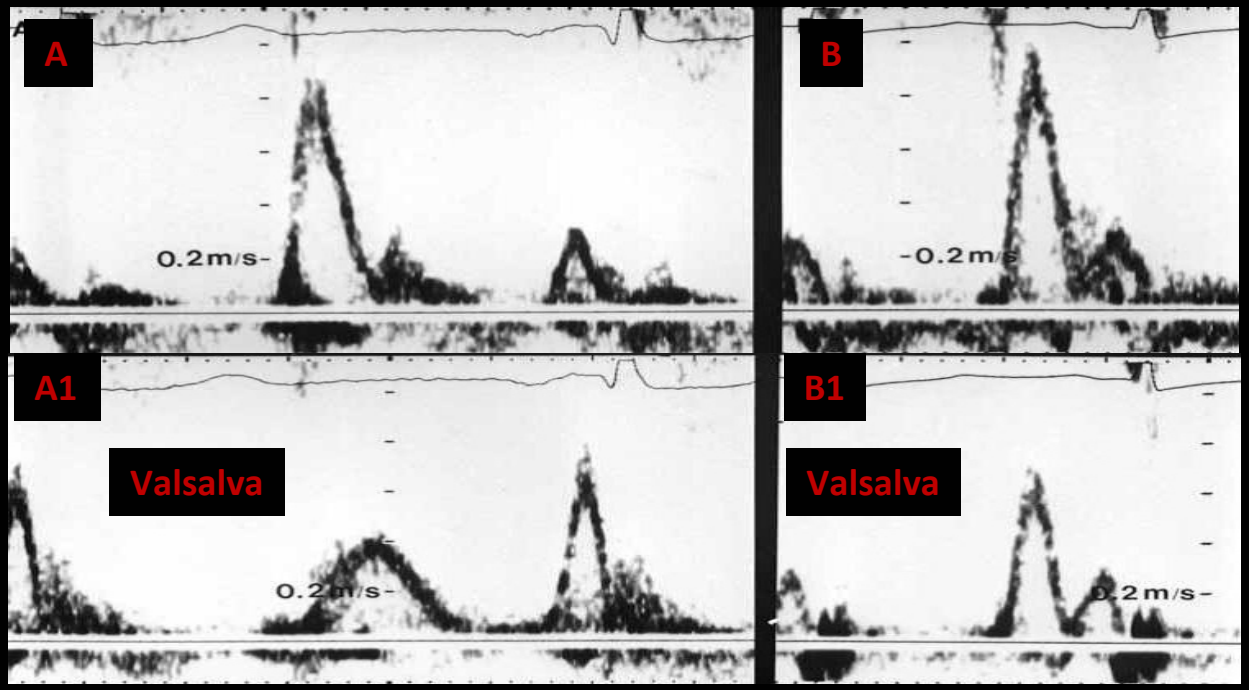
REVERSIBLE RESTRICTIVE FILLING– GRADE III

Mitral Inflow Velocities



- **A** - restrictive filling associated with increased preload in a patient with renal failure
- **B** - After dialysis and decreased LV filling pressure, underlying impaired relaxation (Grade I) is unmasked

IREVERSIBLE RESTRICTIVE FILLING– GRADE IV



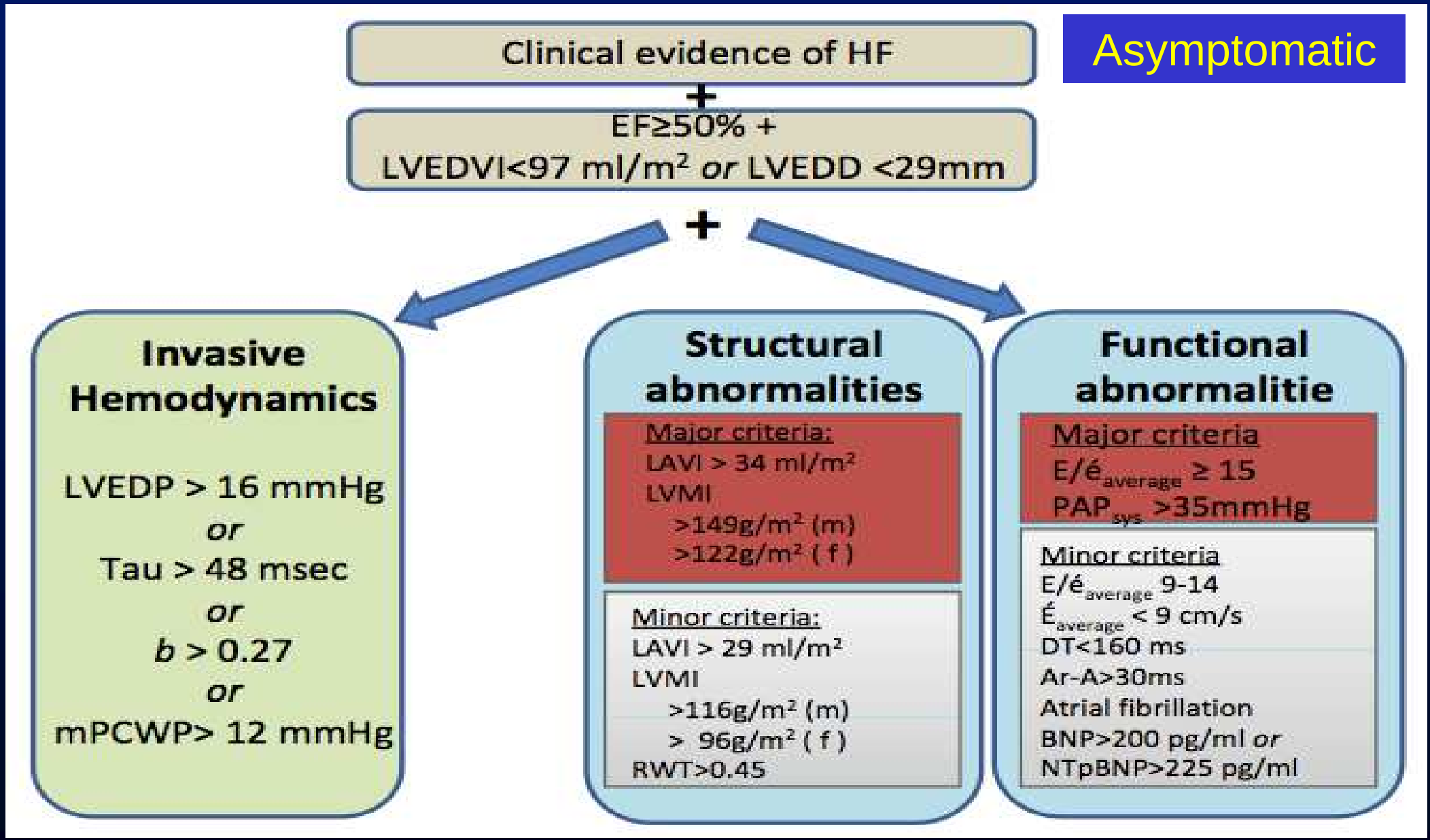
A - restrictive filling pattern at baseline

A1 - restrictive filling after Valsalva's maneuver reverts to Grade 1 DD

B - restrictive filling pattern at baseline

B1 - restrictive filling after Valsalva's maneuver does not reverts - **Irreversible**

HFpEF : NEW DIAGNOSTIC RECOMENDATIONS ?



Burkert Pieske . ESC 2013.

TOPCAT: Trial Design

Funded by the NHLBI

- AGE ≥ 50 YRS
- EF ≥ 45% WITHIN 6 MONTHS
- HEART FAILURE SYMPTOMS AND SIGNS
- CONTROLLED SYSTOLIC BP (< 140 mm Hg)*
- SERUM K^+ ≤ 5.0 MMOL/L

PLUS ONE OF THE FOLLOWING:

- HF HOSPITALIZATION WITHIN 12 MONTHS
- BNP ≥ 100 PG/ML
- N-TERMINAL PRO-BNP ≥ 360 PG/ML

N=3500

↓

RANDOMIZE

↓

PLACEBO 15 MG | **SPIRONOLACTONE 15 MG**

Week 0

↓

DOSE TITRATION (TARGET 30 MG)
**** Optional Titration to 45 mg at 4 mos***

Week 4

↓

COMPOSITE PRIMARY ENDPOINT
CV death, Aborted cardiac arrest, Hospitalization for management of HF

~ 3.25 yrs

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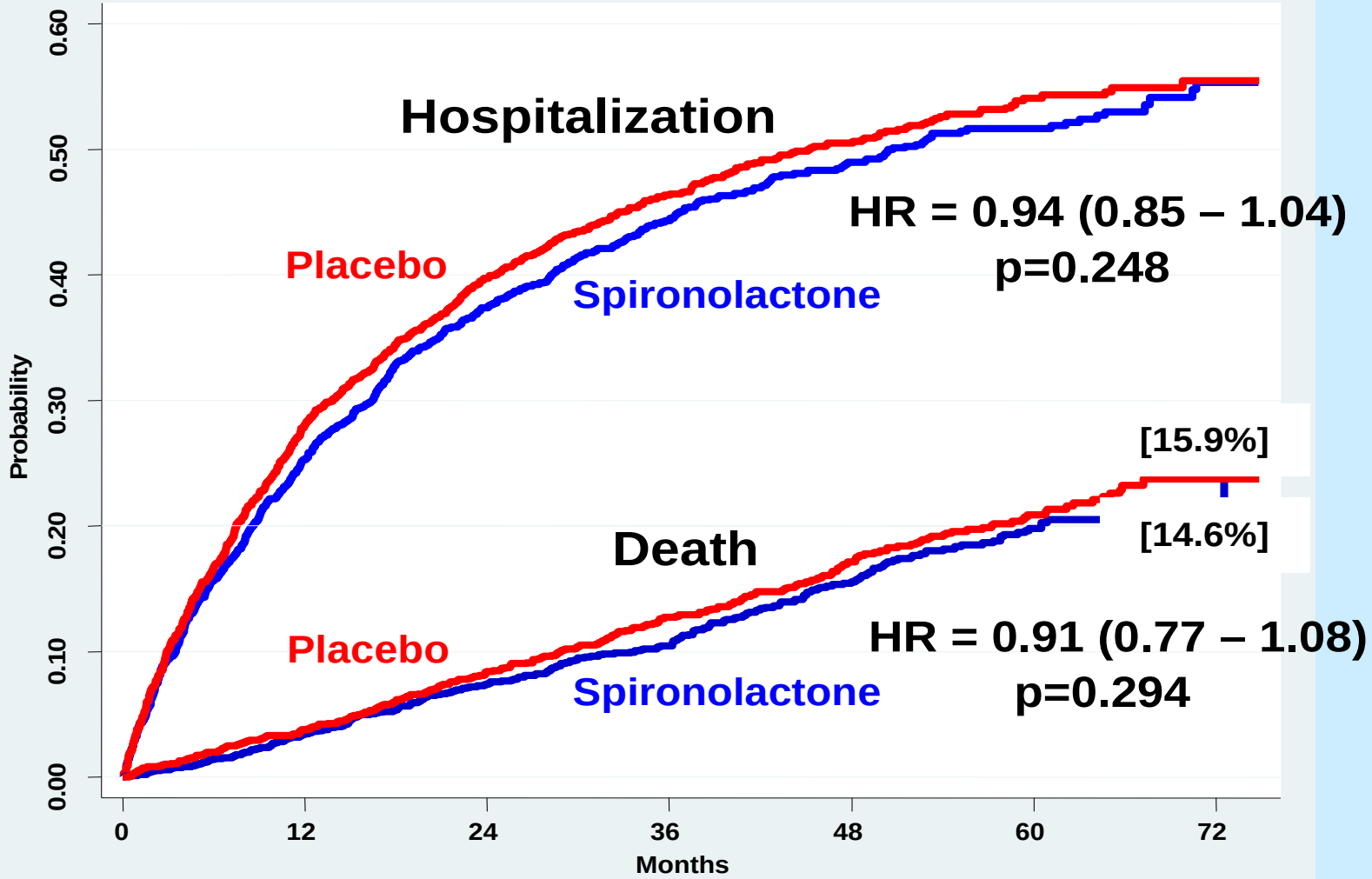
TOPCAT

Deaths, Hospitalization – all causes



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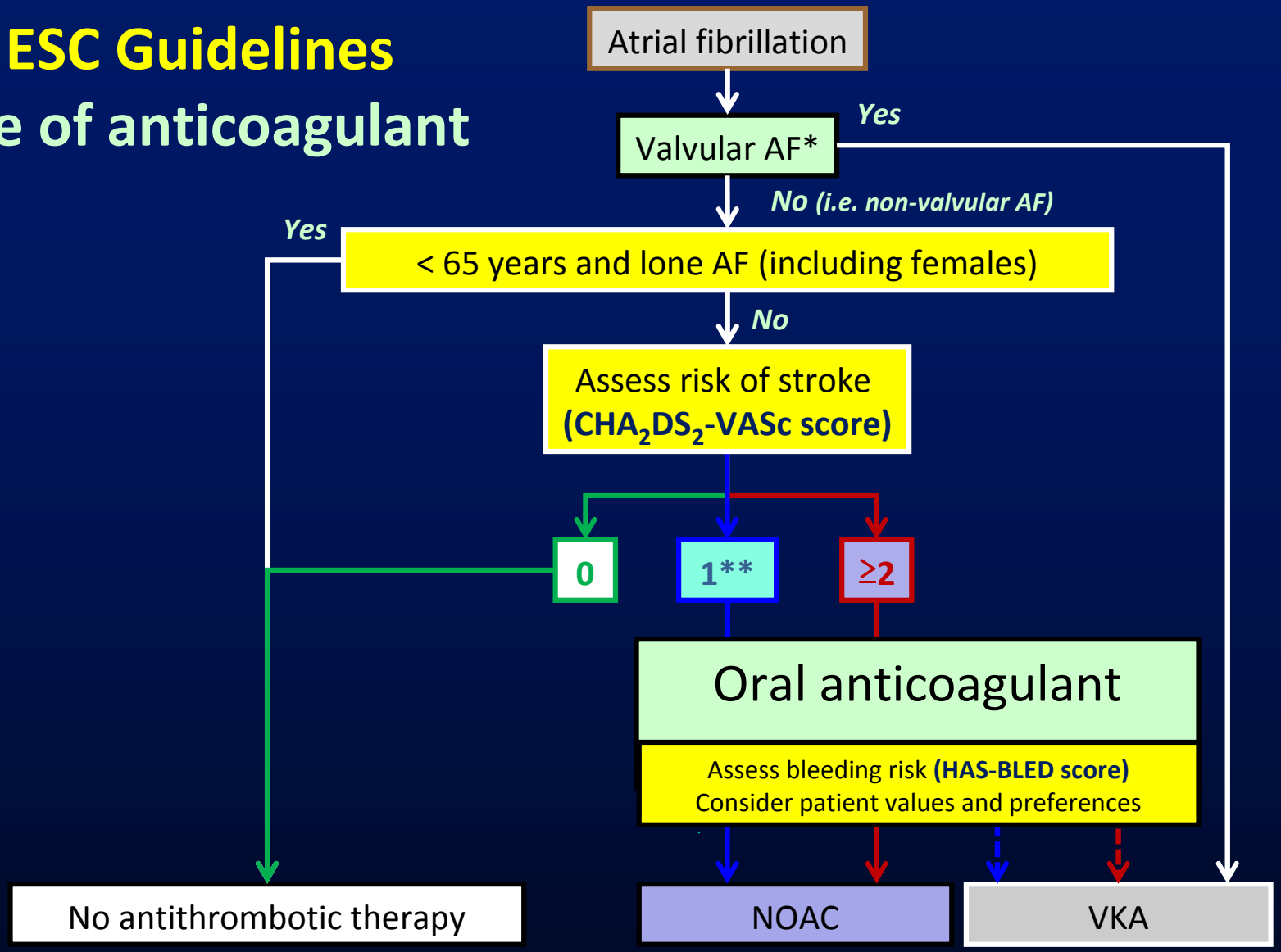
AF ESC Guidelines
Choice of anticoagulant



* Includes rheumatic valvular AF, hypertrophic cardiomyopathy, etc.

** Antiplatelet therapy with aspirin plus clopidogrel, or – less effectively – aspirin only, may be considered in patients who refuse any OAC.

Colour: CHA_2DS_2-VASc score; green = 1, blue = 2, red = ≤2. Line: Solid: best option; Dashed: alternative option.

If absolute contraindications to any OAC or anti-platelet therapy, left atrial appendage closure device can be considered.

AF = atrial fibrillation; CHA_2DS_2-VASc = see text; HAS-BLED = see text; NOAC = novel anticoagulants; VKA = vitamin K antagonist.

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ORAL ANTICOAGULANTS
Phase III AF Trials

	Re-LY	ROCKET-AF	ARISTO TLE	ENGAGE AF-TIMI 48
Drug	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Dose (mg) Freq	150, 110 BID	20 (15*) QD	5 (2.5*) BID	60*, 30* QD
N	18,113	14,266	18,206	>21,000
Design	PROBE	2x blind	2x blind	2x blind
AF criteria	AF x 1 < 6 mths	AF x 2 (≥1 in <30d)	AF or AFl x 2 <12 mths	AF x 1 < 12 mths
% VKA naive	50%	38%	43%	40% goal

*Dose adjusted in patients with ↓ drug clearance. **Max of 10% with CHADS-2 score = 2 and no stroke/TIA/SEE

PROBE = prospective, randomized, open-label, blinded end point evaluation VKA = Vitamin K antagonist

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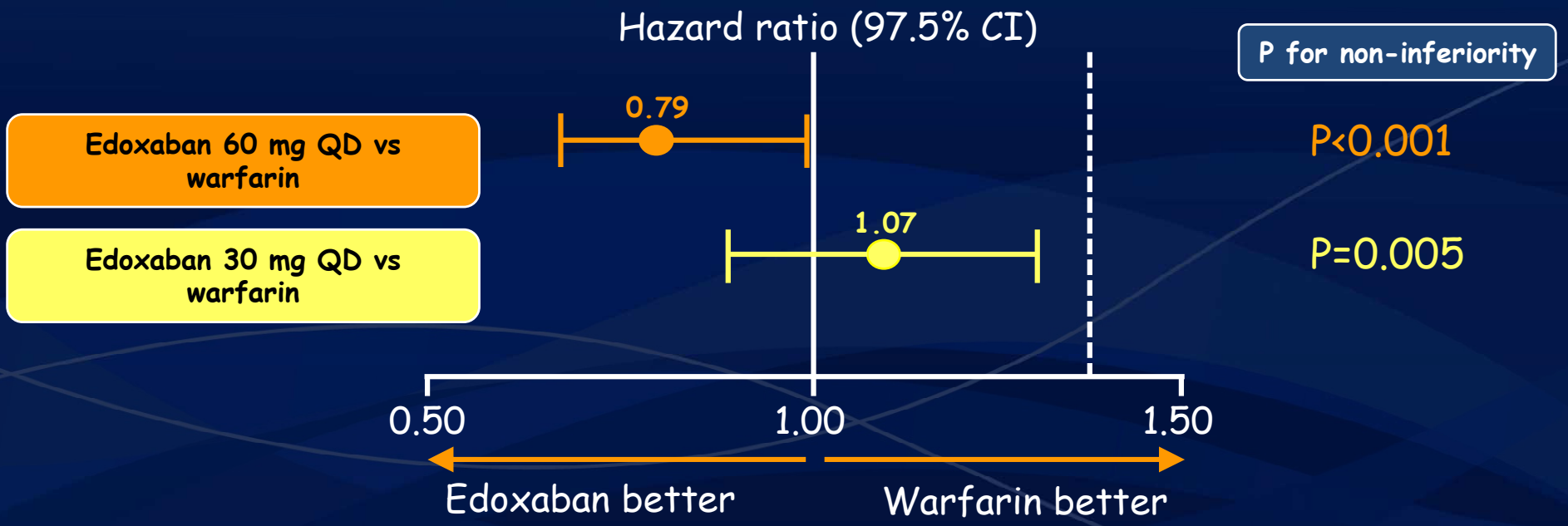
Primary efficacy endpoint: stroke or SEE mITT on-treatment analysis

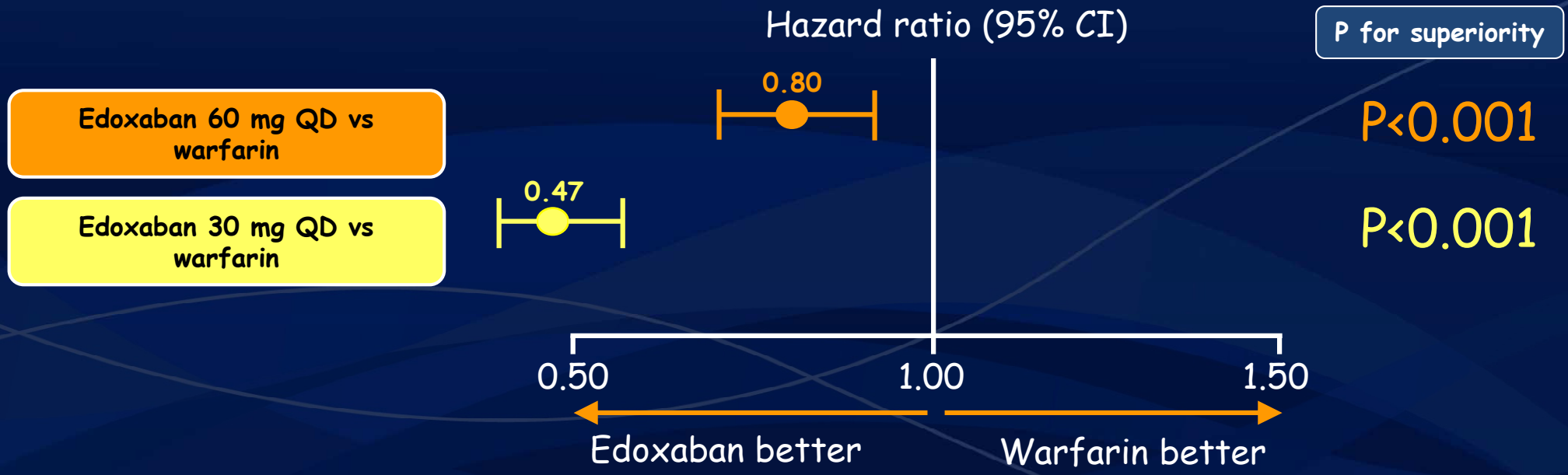
				Edoxaban versus warfarin	
Treatment	**N**	**n**	**Incidence (%/yr)**	**HR (97.5% CI)**	**P for non-inferiority**
Warfarin (median TTR 68.4%)	7,012	232	1.50	-	-
Edoxaban 60 mg QD	7,012	182	1.18	0.79 (0.63–0.99)	P<0.001
Edoxaban 30 mg QD	7,002	253	1.61	1.07 (0.87–1.31)	0.005



Giugliano et al. N Engl J Med 2013; e-pub ahead of print

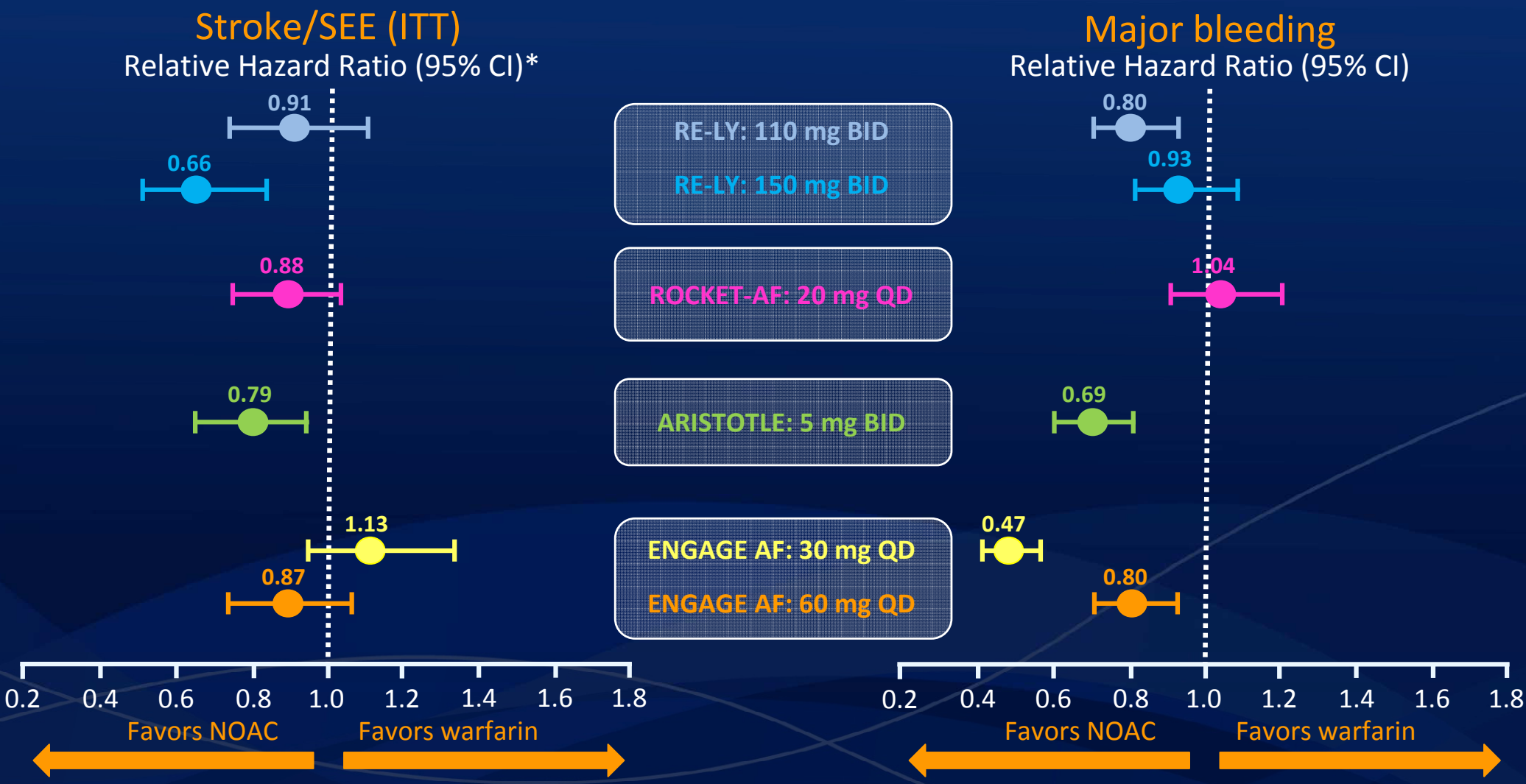
Major bleeding
Safety on-treatment analysis

				Edoxaban versus warfarin	
Treatment	**N**	**n**	**Incidence (%/yr)**	**HR (95% CI)**	**P value**
Warfarin	7,012	524	3.43	-	-
Edoxaban 60 mg QD	7,012	418	2.75	0.80 (0.71–0.91)	<0.001
Edoxaban 30 mg QD	7,002	254	1.61	0.47 (0.41–0.55)	<0.001



Giugliano et al. N Engl J Med 2013; e-pub ahead of print

AF trials: summary results

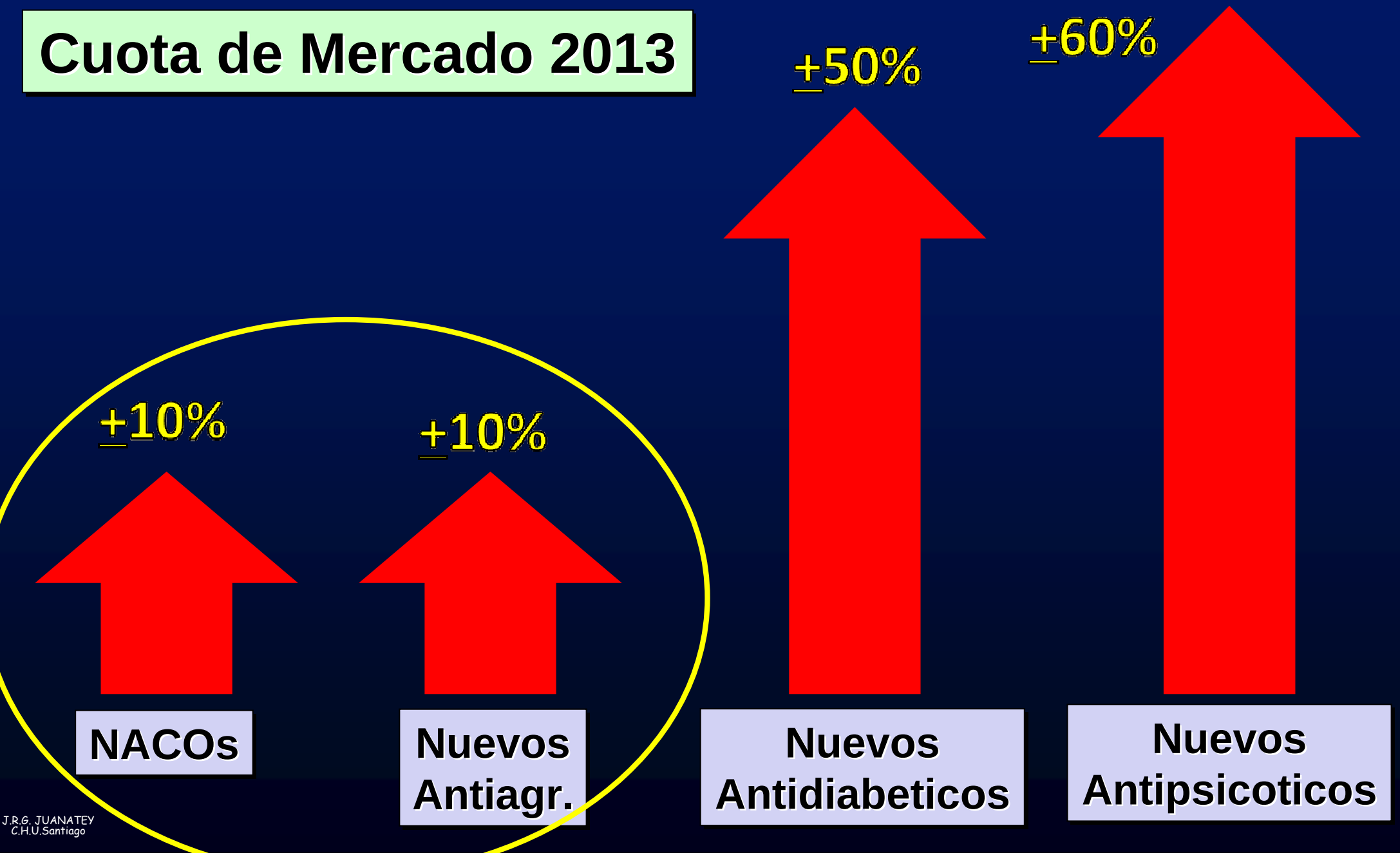


*97.5% CI for ENGAGE AF

1. Connolly et al. N Engl J Med 2009;361:1139–1151; 2. Patel et al. N Engl J Med 2011;365:883–891
3. Granger et al. N Engl J Med 2011;365:981–992; 4. Giugliano et al. N Engl J Med 2013; e-pub ahead of print

Empleo de NACOs vs Otros Nuevos Tratamientos

Cuota de Mercado 2013



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