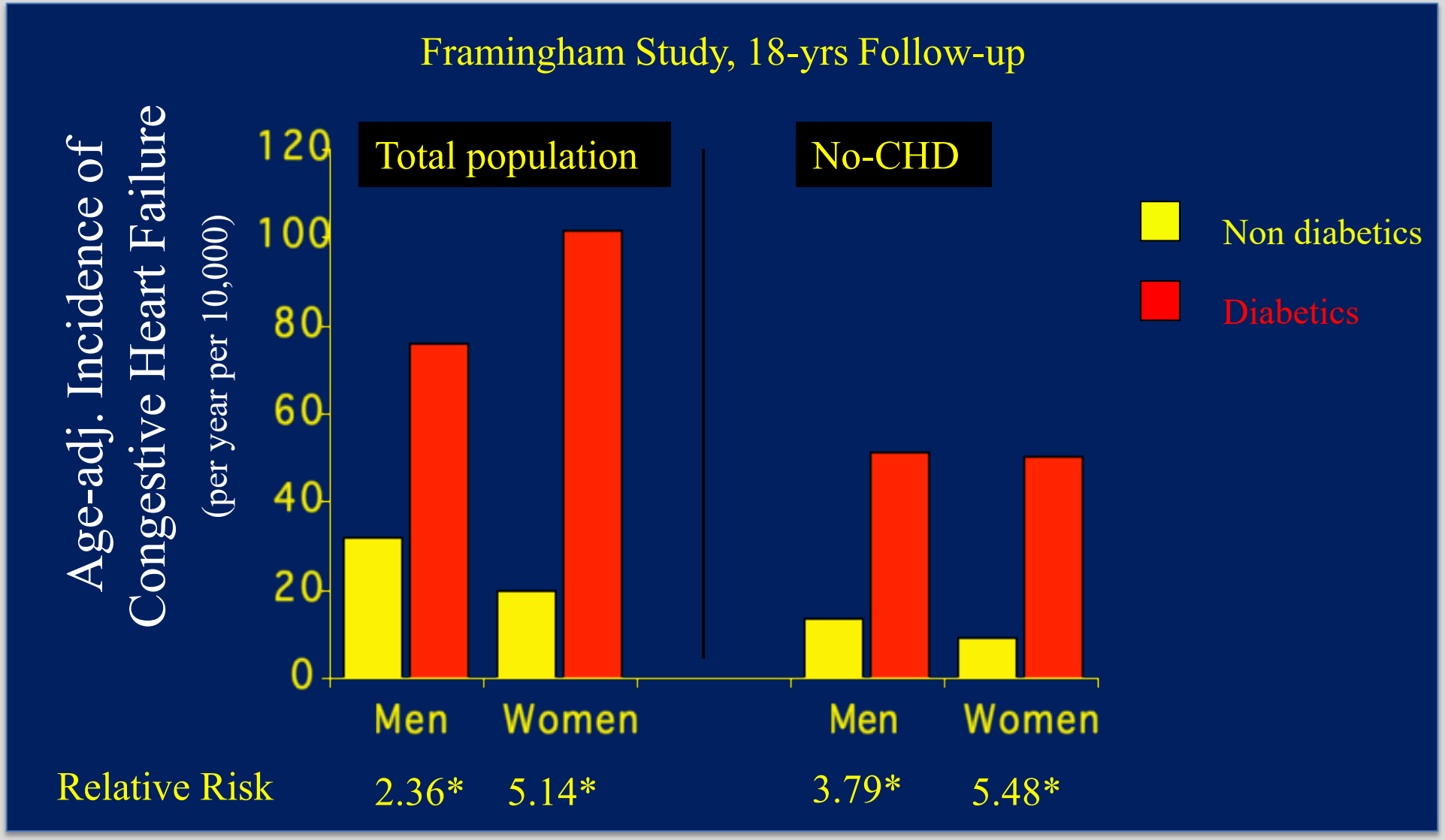
Scompenso cardiaco: la riscoperta della cenerentola delle complicanze cardiovascolari del diabete

Andrea Natali (Pisa)

Già si sapeva (1979) !



Kannel WB, JAMA 1979


SGLT2i

ESC and ADA/JAAC Position statements

European Journal of Heart Failure (2018) **20**, 853–872
doi:10.1002/ejhf.1170

HFA POSITION STATEMENT

Type 2 diabetes mellitus and heart failure: a position statement from the Heart Failure Association of the European Society of Cardiology

Petar M. Seferović[1]*, Mark C. Petrie[2], Gerasimos S. Filippatos[3], Stefan D. Anker[4], Giuseppe Rosano[5], Johann Bauersachs[6], Walter J. Paulus[7], Michel Komajda[8], Francesco Cosentino[9], Rudolf A. de Boer[10], Dimitrios Farmakis[2], Wolfram Doehner[11], Ekaterini Lambrinou[12], Yuri Lopatin[13], Massimo F. Piepoli[14], Michael J. Theodorakis[15], Henrik Wiggers[16], John Lekakis[2], Alexandre Mebazaa[17], Mamas A. Mamas[18], Carsten Tschöpe[19], Arno W. Hoes[20], Jelena P. Seferović[21], Jennifer Logue[22], Theresa McDonagh[23], Jillian P. Riley[24], Ivan Milinković[1], Marija Polovina[1], Dirk J. van Veldhuisen[25], Mitja Lainscak[26], Aldo P. Maggioni[27], Frank Ruschitzka[28], and John J.V. McMurray[29]

Check for updates

Heart Failure: An Underappreciated Complication of Diabetes. A Consensus Report of the American Diabetes Association

Rodica Pop-Busui,[1] James L. Januzzi,[2] Dennis Bruemmer,[3] Sonia Butalia,[4] Jennifer B. Green,[5] William B. Horton,[6] Colette Knight,[7] Moshe Levi,[8] Neda Rasouli,[9] and Caroline R. Richardson[10]

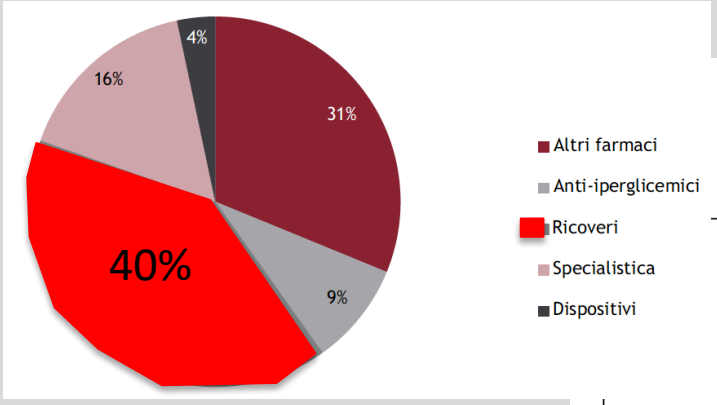
Diabetes Care 2022;45:1670–1690 | https://doi.org/10.2337/dci22-0014

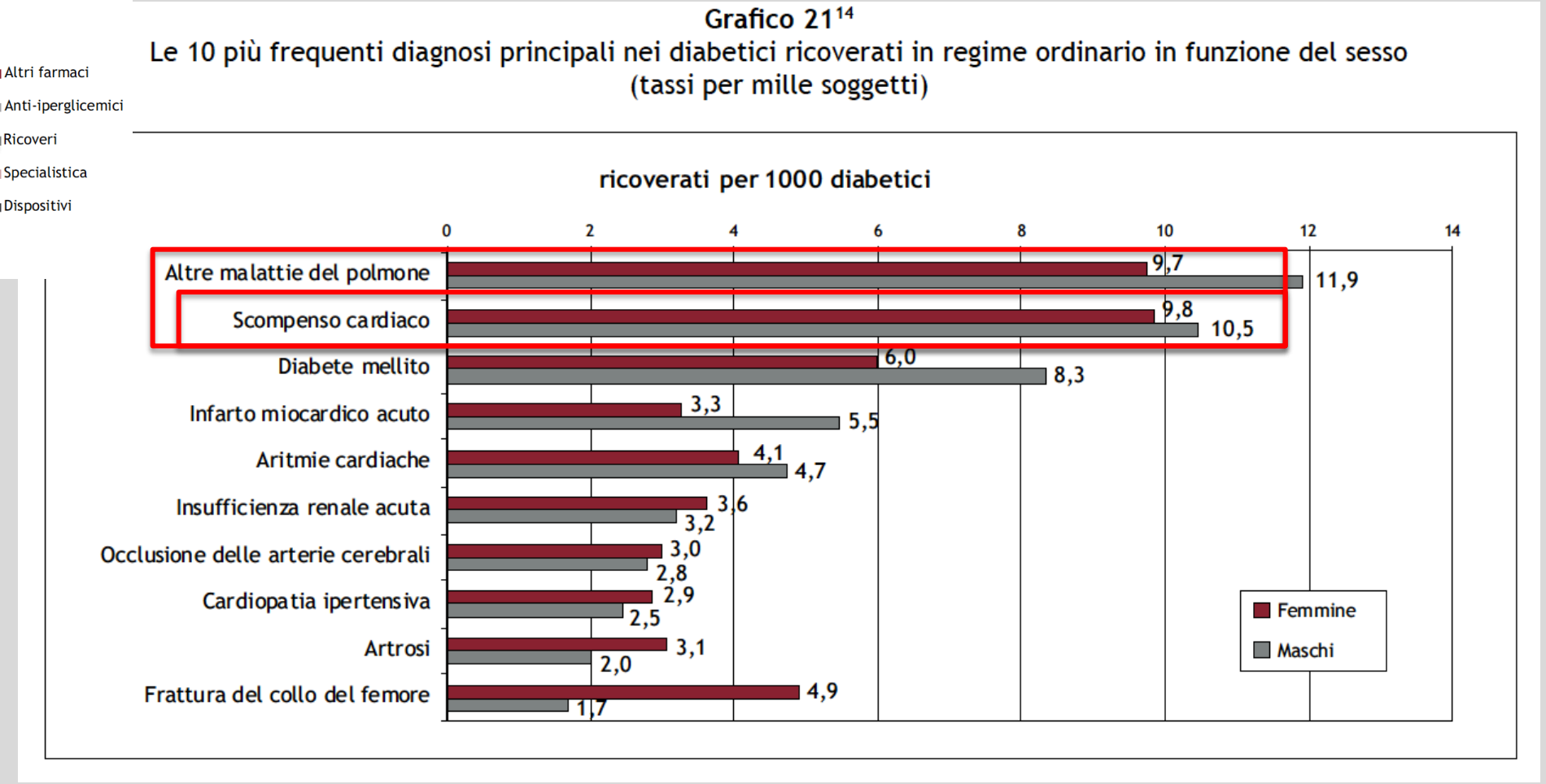
Outline

- Dimensione del problema
- Definizioni, storia naturale e fenotipi
- Come trovare i pazienti a rischio
- Cosa fare e non fare una volta che li abbiamo trovati

Diabete & HHF: italia

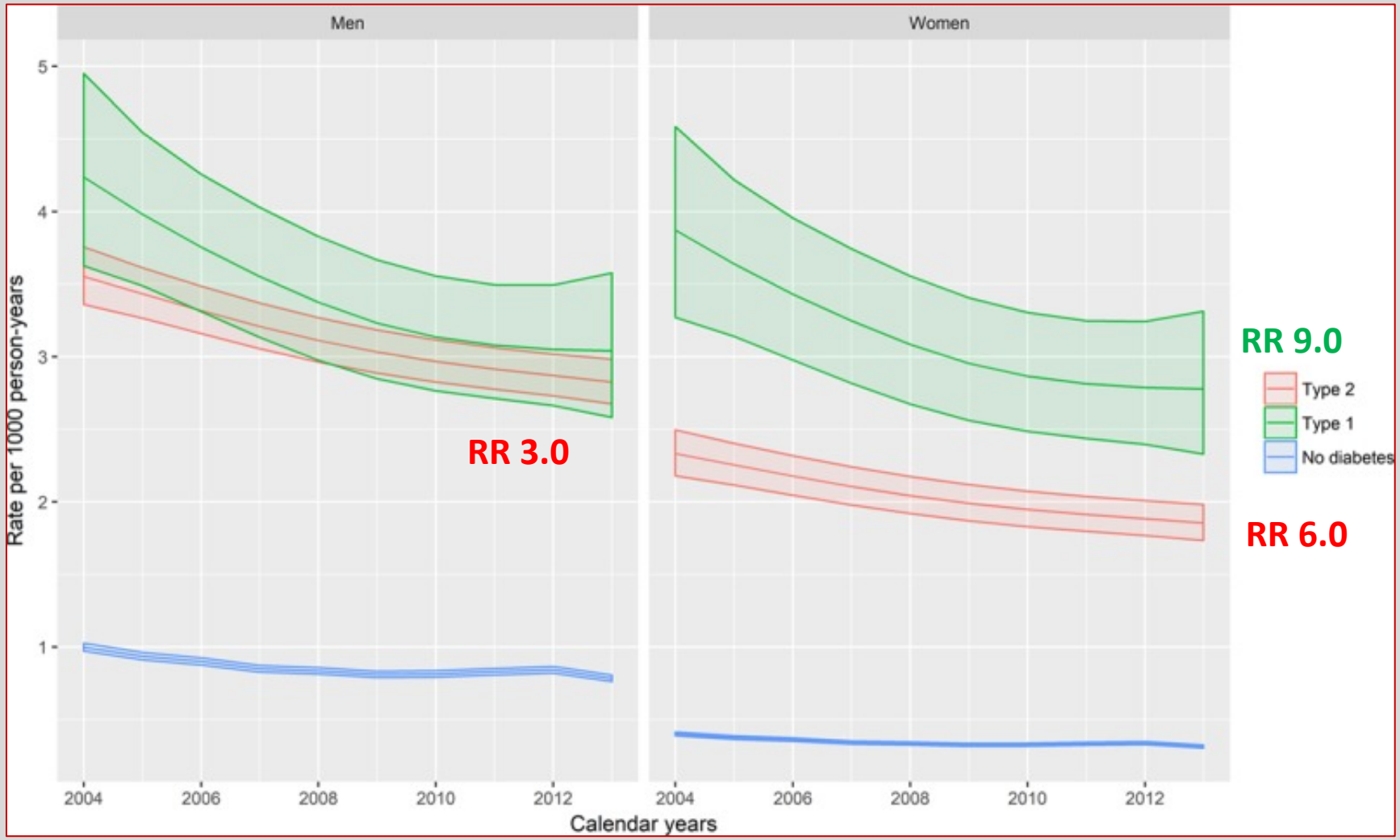
€ 2.833/anno/pt





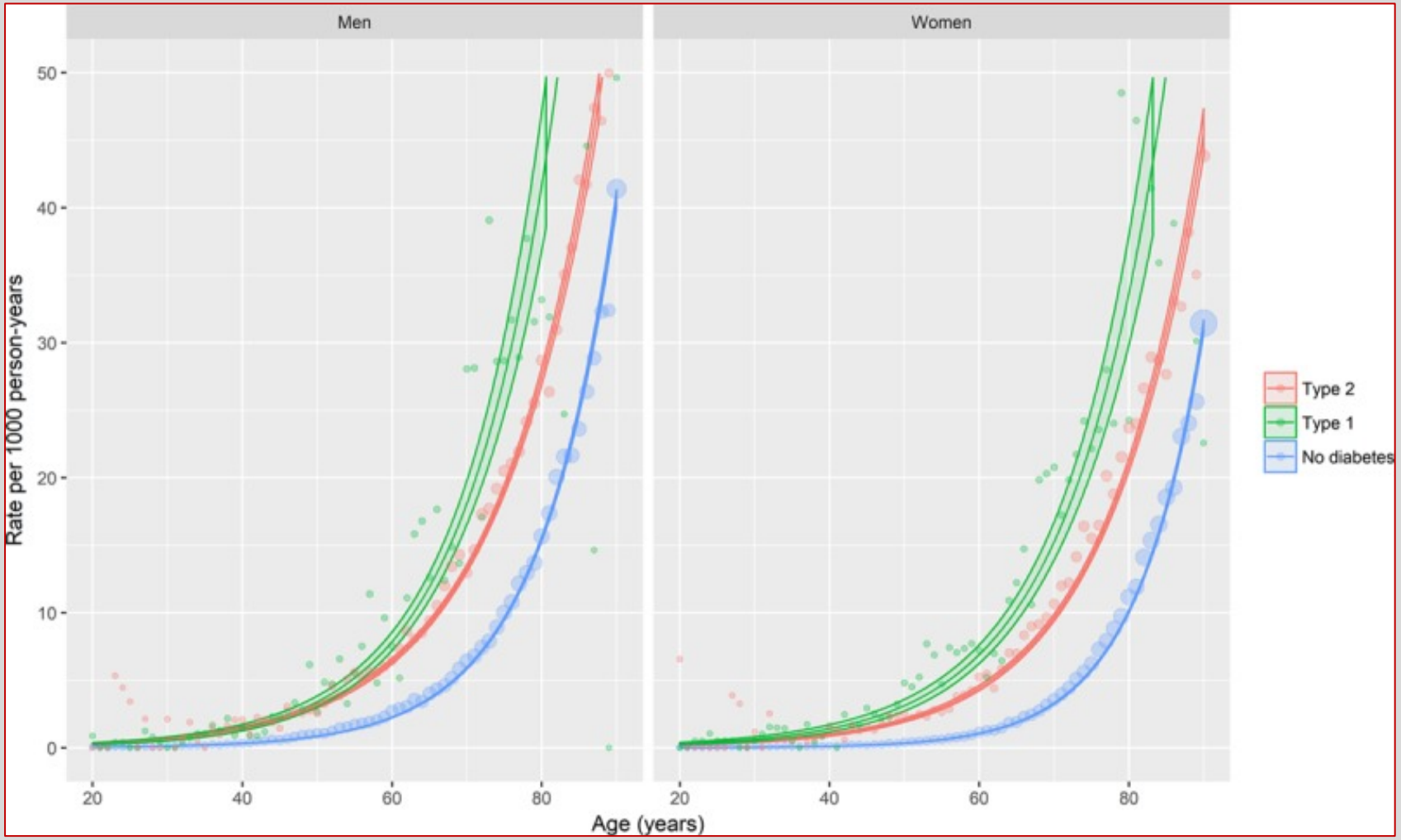
Incidenza di HHF nel diabete 1 & 2 (2004-14)

Scozia (3.25 M)
136,042 T2D
18,240 T1D



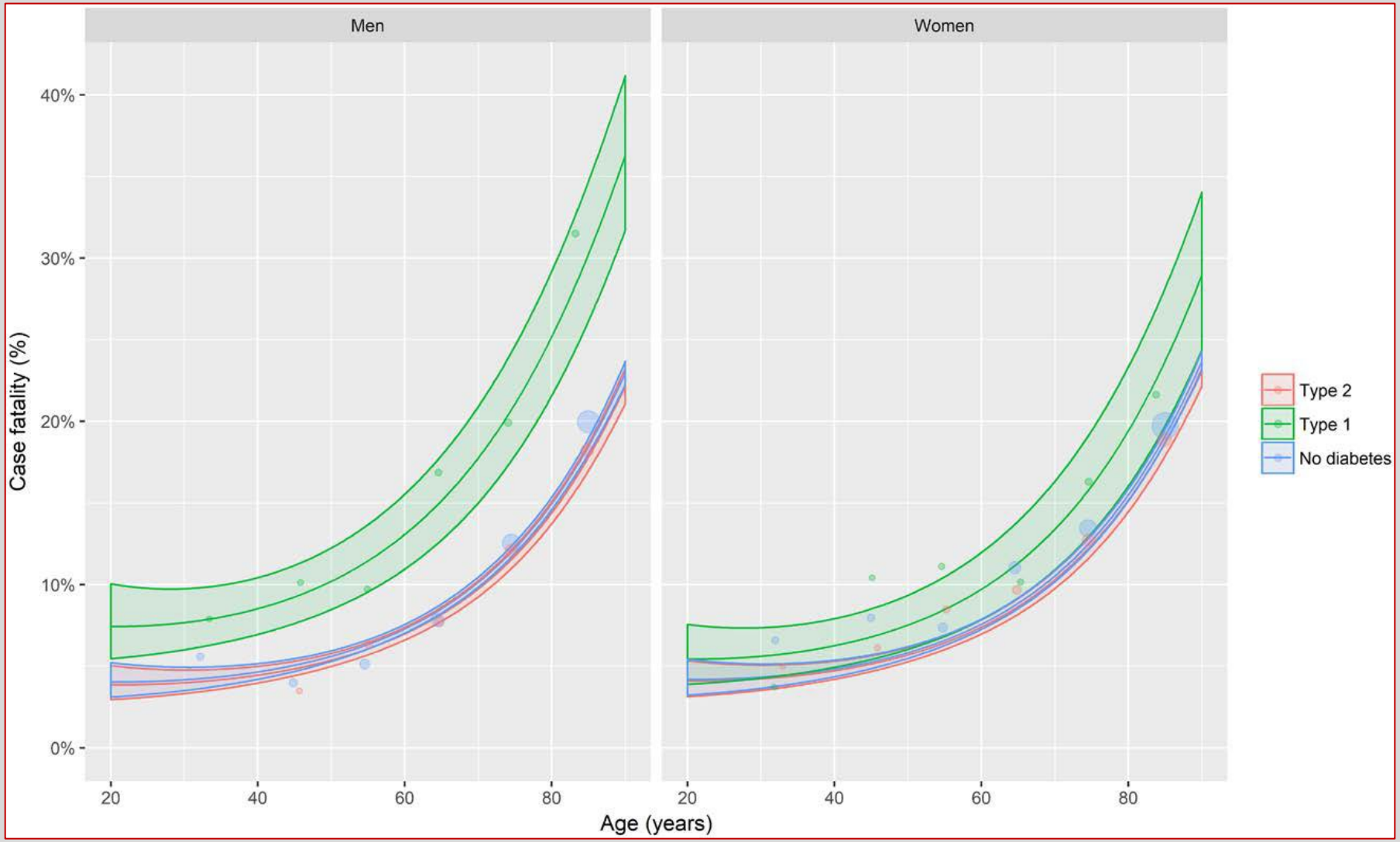
McAllister DA et al *Circulation* 2018

Diabete & HHF: anticipa di 10 anni la dx



McAllister DA et al *Circulation* 2018

Diabete & HHF: = mortalità a 30gg

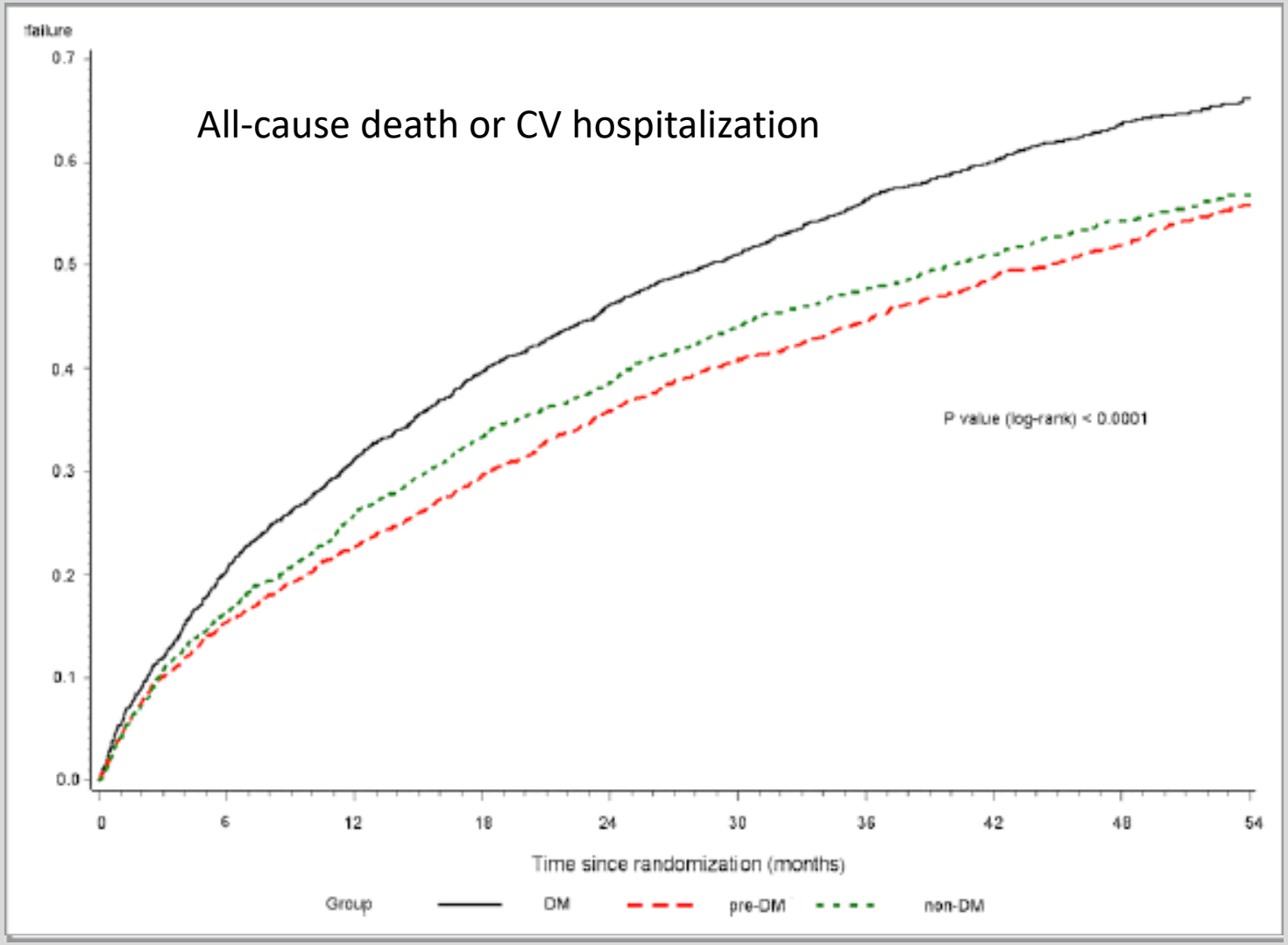


McAllister DA et al *Circulation* 2018

Diabetes and pre-diabetes & HF outcomes (GISSI)

N=6,935 (78.3% men)
amb. patients with CHF
Age 67+/-11
LVEF 33+/-8
41% DM (Known 28%)
29% PreD (HbA1c 6-6.4%)

Among Diab
HbA1c >7.5 vs <6.5
All cuse death
RR 1.22 [1.02-1.43]



Dauriz M et al Am J Heart Assoc 2017

Outline

- Dimensione del problema
- **Definizioni, storia naturale e fenotipi**
- Come trovare i pazienti a rischio
- Cosa fare e non fare una volta che li abbiamo trovati

Definizioni

Insufficienza cardiaca (Heart failure)

Sindrome clinica complessa e progressiva risultante dall'incapacità del cuore di mantenere la propria funzione (perfusione tissutale) indipendentemente dalla natura del danno iniziale. E' una condizione cronica in cui i meccanismi fisiologici ed i farmaci riescono a mantenere un normale/soddisfacente compenso emodinamico.

Scompenso cardiaco (Decompensated HF)

Condizione acuta o subacute in cui si perde il normale compenso emodinamico con sofferenza di organi o tessuti.

Sintomi di scompenso cardiaco

2 maggiori

1 maggiore + 2 minori

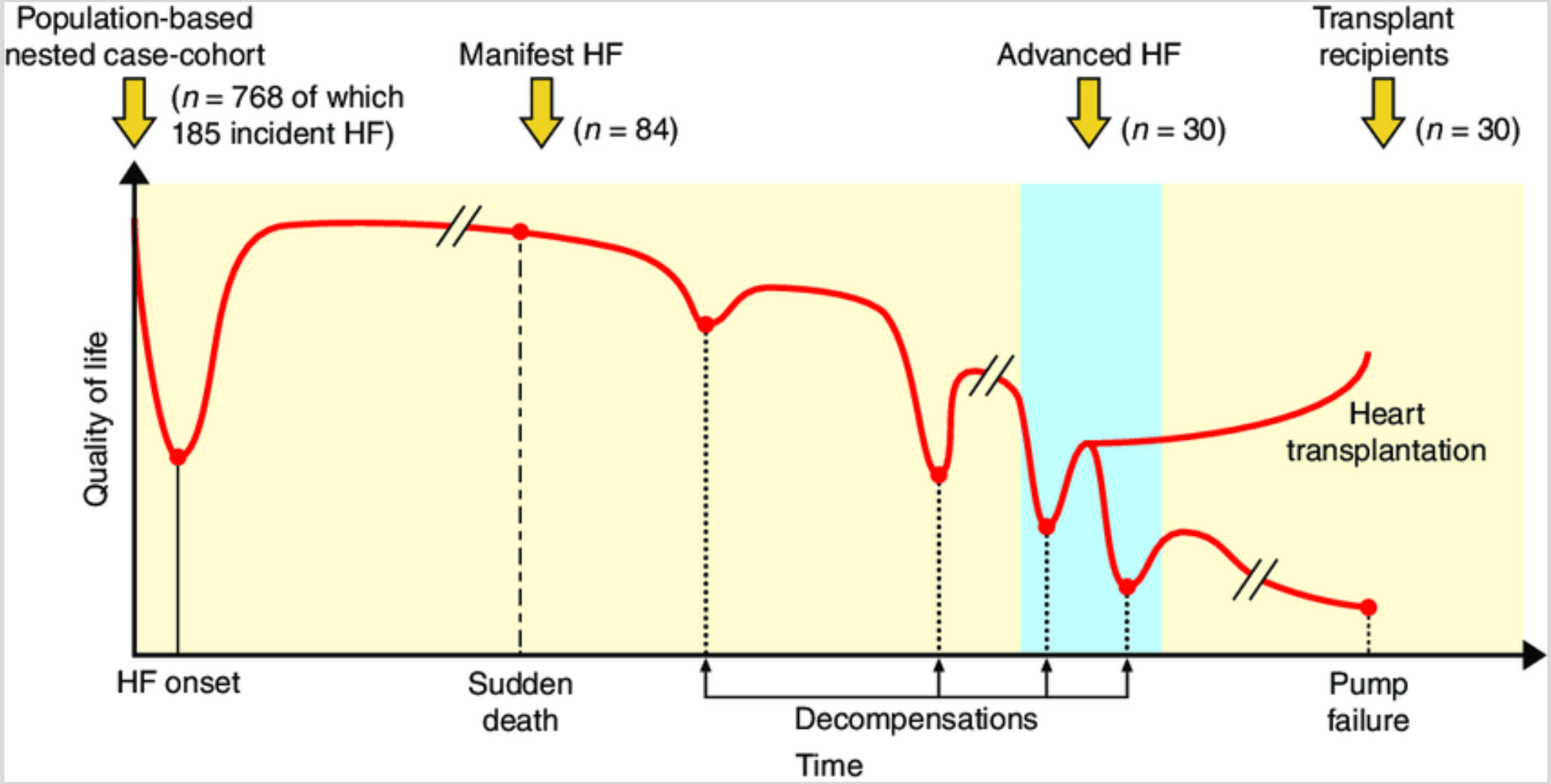
Table 6. Framingham Diagnostic Criteria for Heart Failure*

Major criteria	Minor criteria
Acute pulmonary edema	Ankle edema
Cardiomegaly	Dyspnea on exertion
Hepatojugular reflex	Hepatomegaly
Neck vein distension	Nocturnal cough
Paroxysmal nocturnal dyspnea or orthopnea	Pleural effusion
Rales	Tachycardia (> 120 beats per minute)
Third heart sound gallop	

**—Heart failure is diagnosed when two major criteria or one major and two minor criteria are met.*

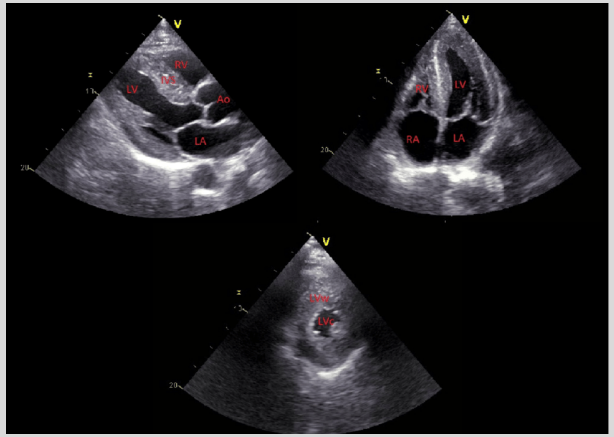
Adapted with permission from Maestre A, Gil V, Gallego J, Aznar J, Mora A, Martin-Hidalgo A. Diagnostic accuracy of clinical criteria for identifying systolic and diastolic heart failure: cross-sectional study. J Eval Clin Pract. *2009;15(1):60.*

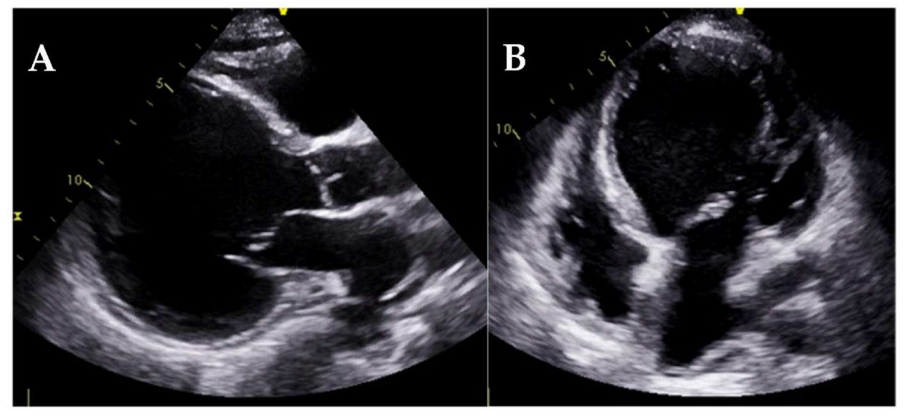
Storia naturale HF



Egerstedt, 2019, Nature comm

Fenotipi di HF





65
60
55
50
45
40
35
30
25
20

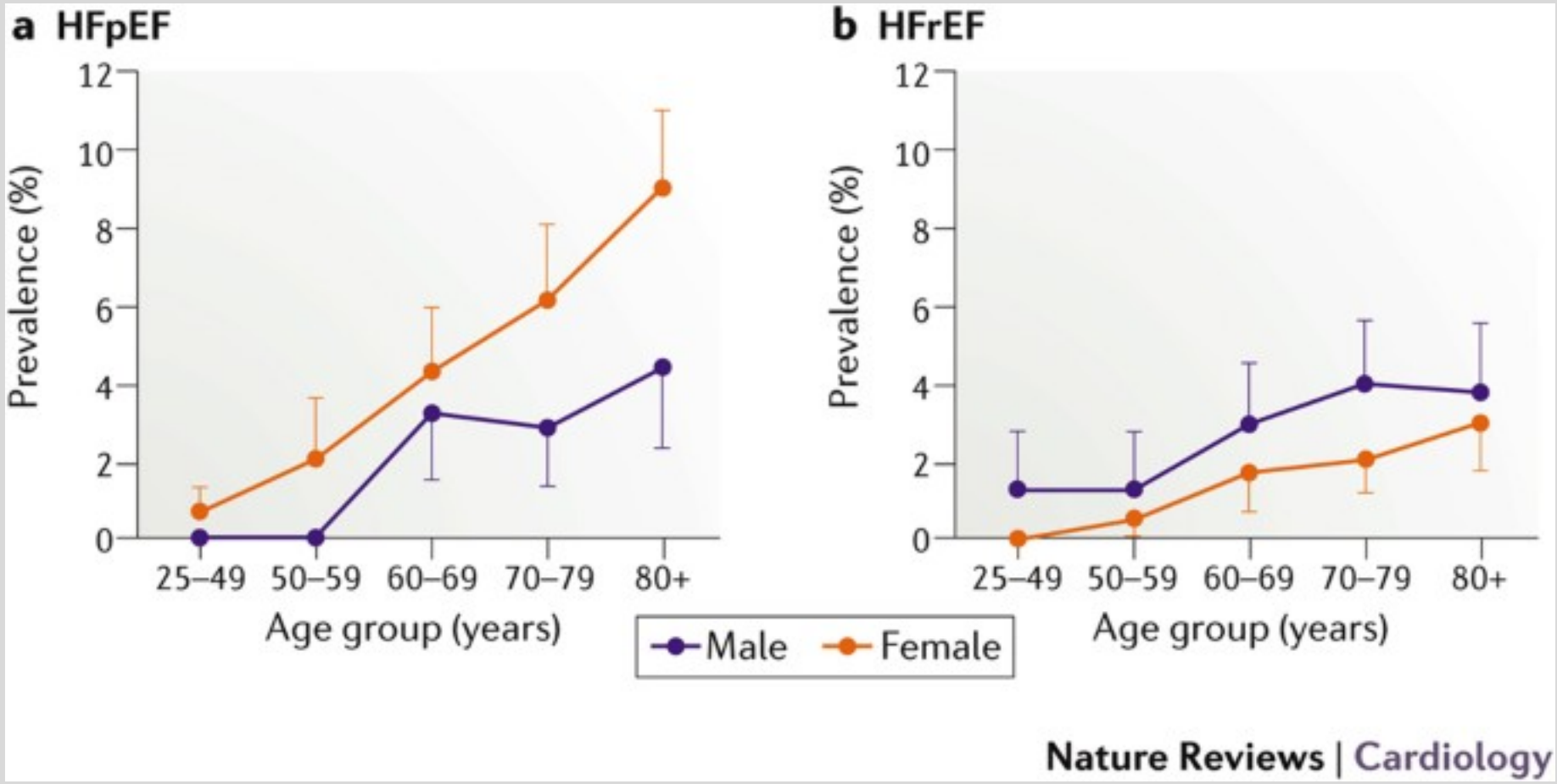
Disfunzione diastolica
&
sistolica subclinica

Non chiamatelo scompenso «diastolico»!

Disfunzione sistolica e diastolica

Prevalenza di HFpEF vs HFrEF ed età

European community-based cohort



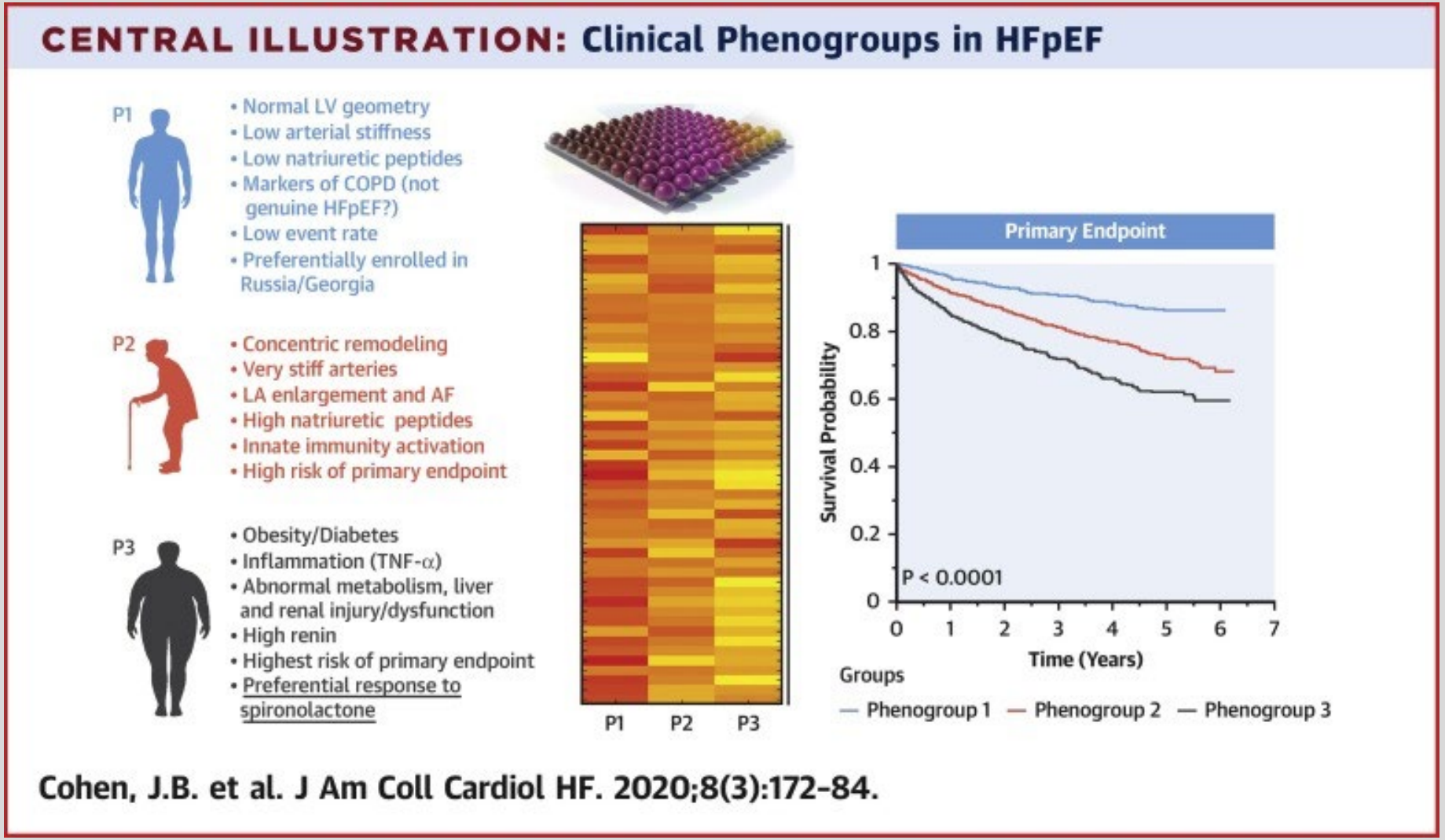
Redrawn from EPICA Study; Eur. J. Heart Fail. **4** (4), 531–539 (2002)

Fenotopi di HFpEF

35%

38%

26%



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- Dimensione del problema
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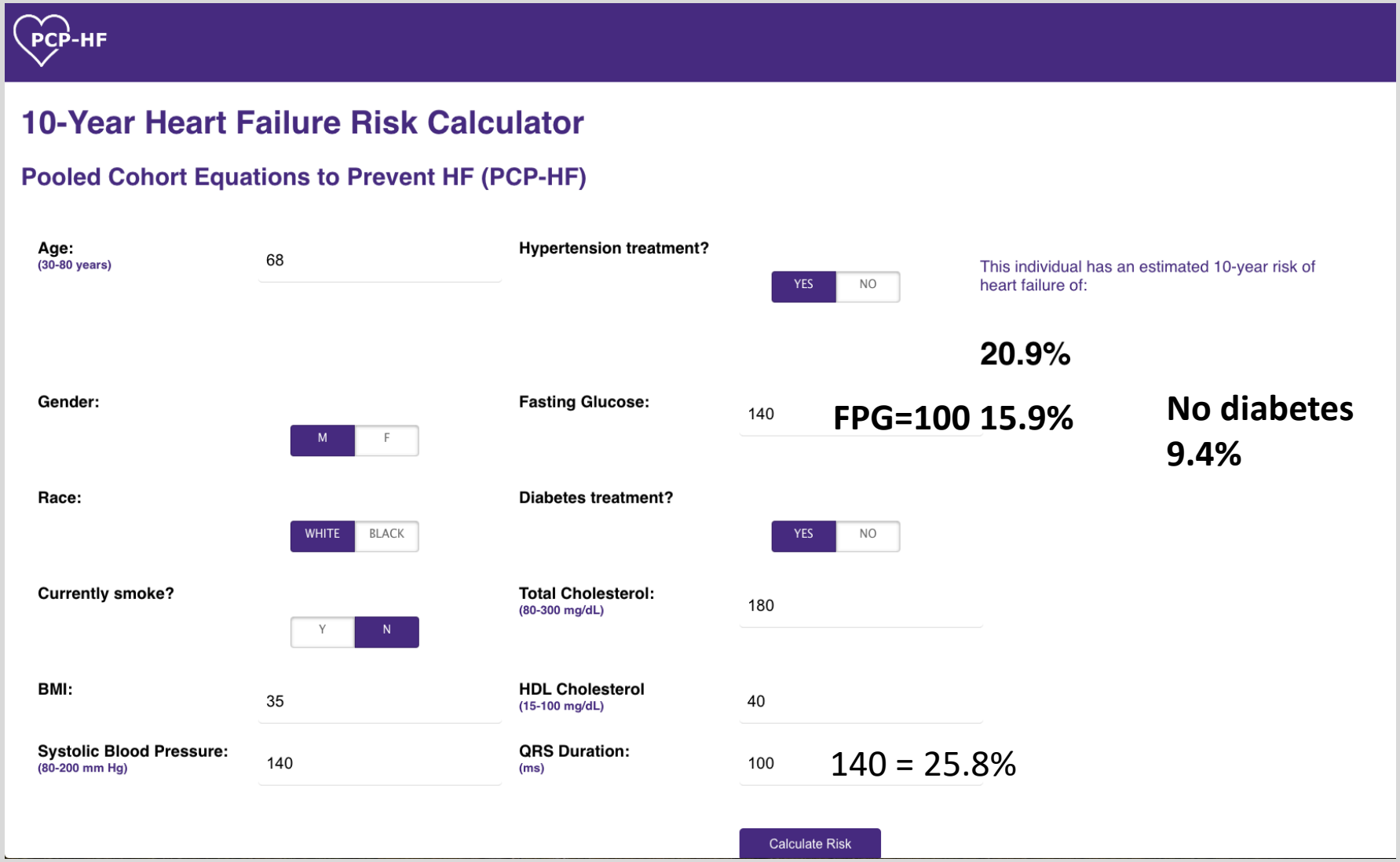
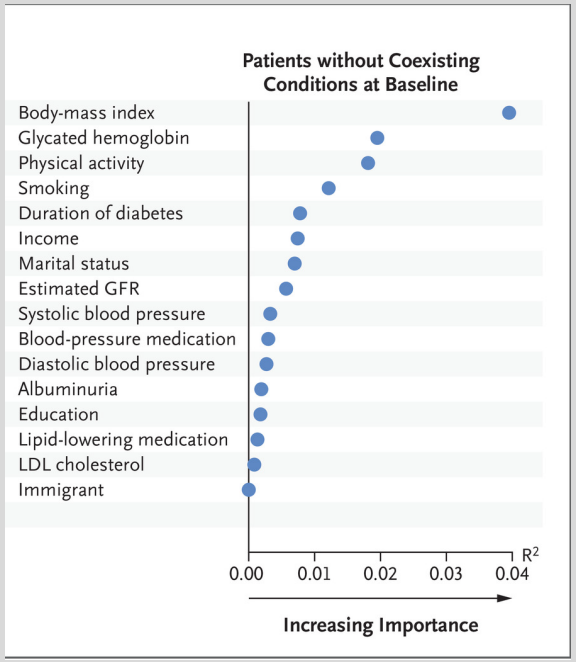
- Cosa fare e non fare una volta che li abbiamo trovati

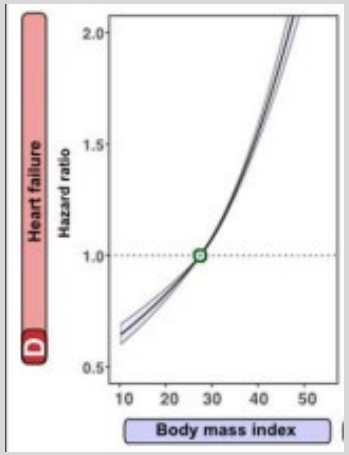
Diabete & HHF: come stimare il rischio individuale

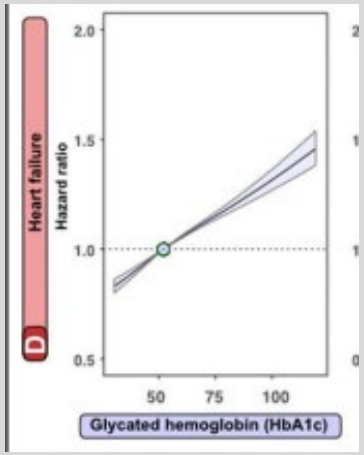


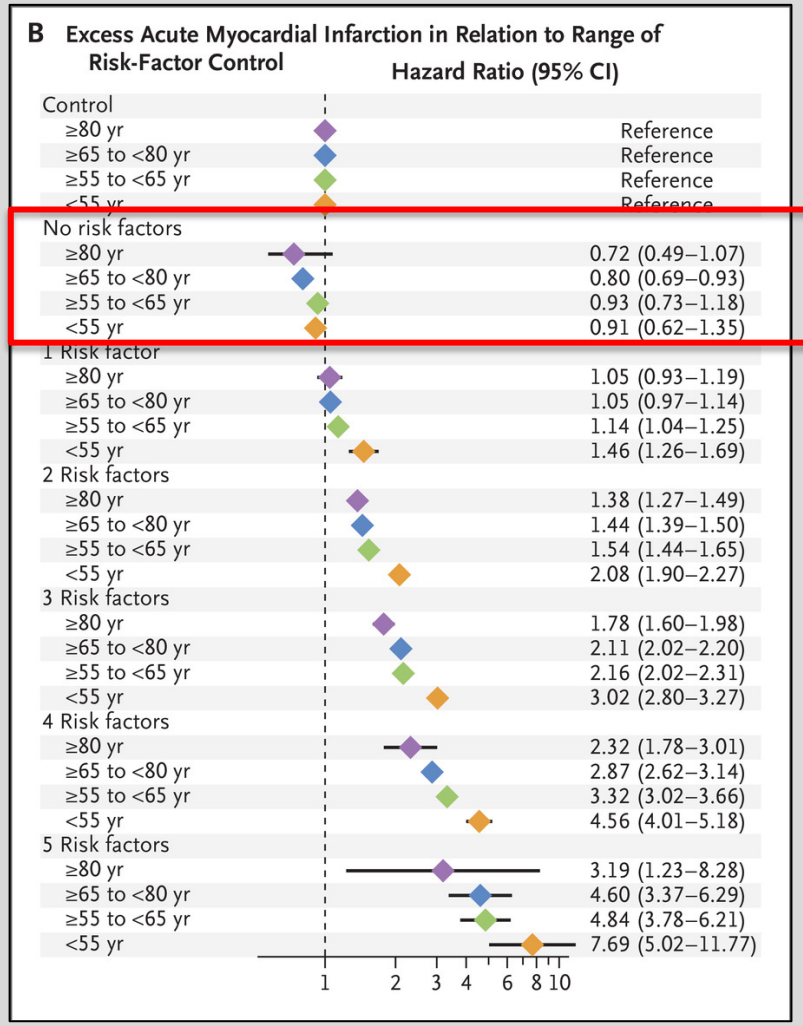
10-Year Heart Failure Risk Calculator Pooled Cohort Equations to Prevent HF (PCP-HF) http://hf-risk-calculator.surge.sh/

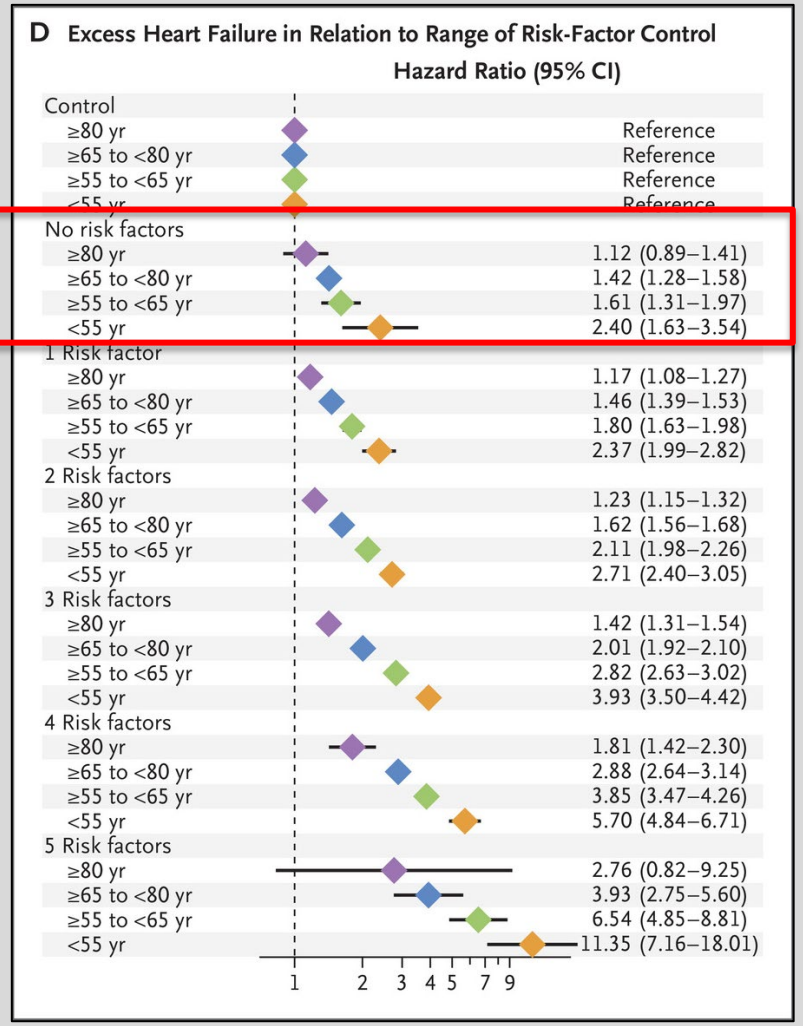
Diabete & rischio di HF vs controllo dei FR











Sattar N, Circulation 2023 and Raswani A, NEJM 2017

HHF: come fare diagnosi precoce (Stage B)

FIGURE 1 ACC/AHA Stages of HF

100%

STAGE A: At-Risk for Heart Failure

Patients at risk for HF but without current or previous symptoms/signs of HF and without structural/ functional heart disease or abnormal biomarkers

Patients with hypertension, CVD, diabetes, obesity, exposure to cardiotoxic agents, genetic variant for cardiomyopathy, or family history of cardiomyopathy

50-60%

STAGE B: Pre-Heart Failure

Patients without current or previous symptoms/signs of HF but evidence of 1 of the following:

Structural heart disease

Evidence of increased filling pressures

Risk factors and
- increased natriuretic peptide levels or
- persistently elevated cardiac troponin

in the absence of competing diagnoses

- Reduced L or R VF
- (Reduced EF, GLS <16, TAPSE <1.5)
- Ventricular hypertrophy
- Chamber enlargement
- Wall motion abnormalities
- Valvular heart disease

NTproBNP ≥125 pg/mL

10%

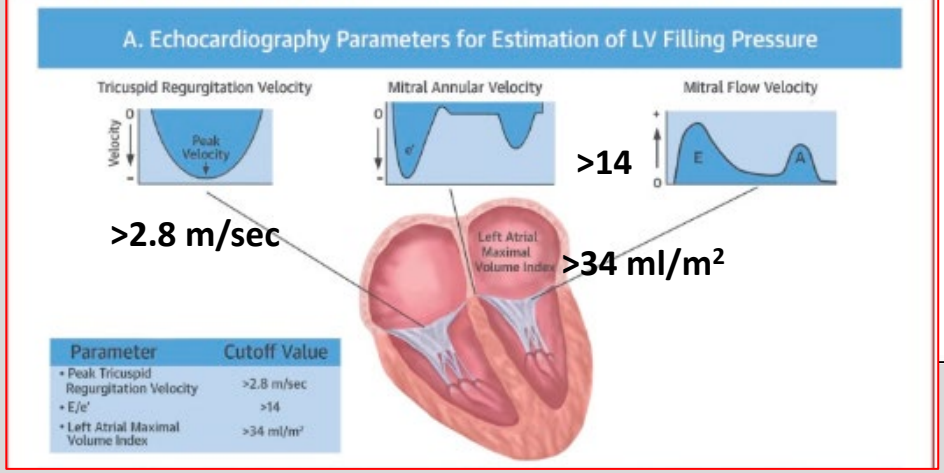
STAGE C: Symptomatic Heart Failure

Patients with current or previous symptoms/signs of HF

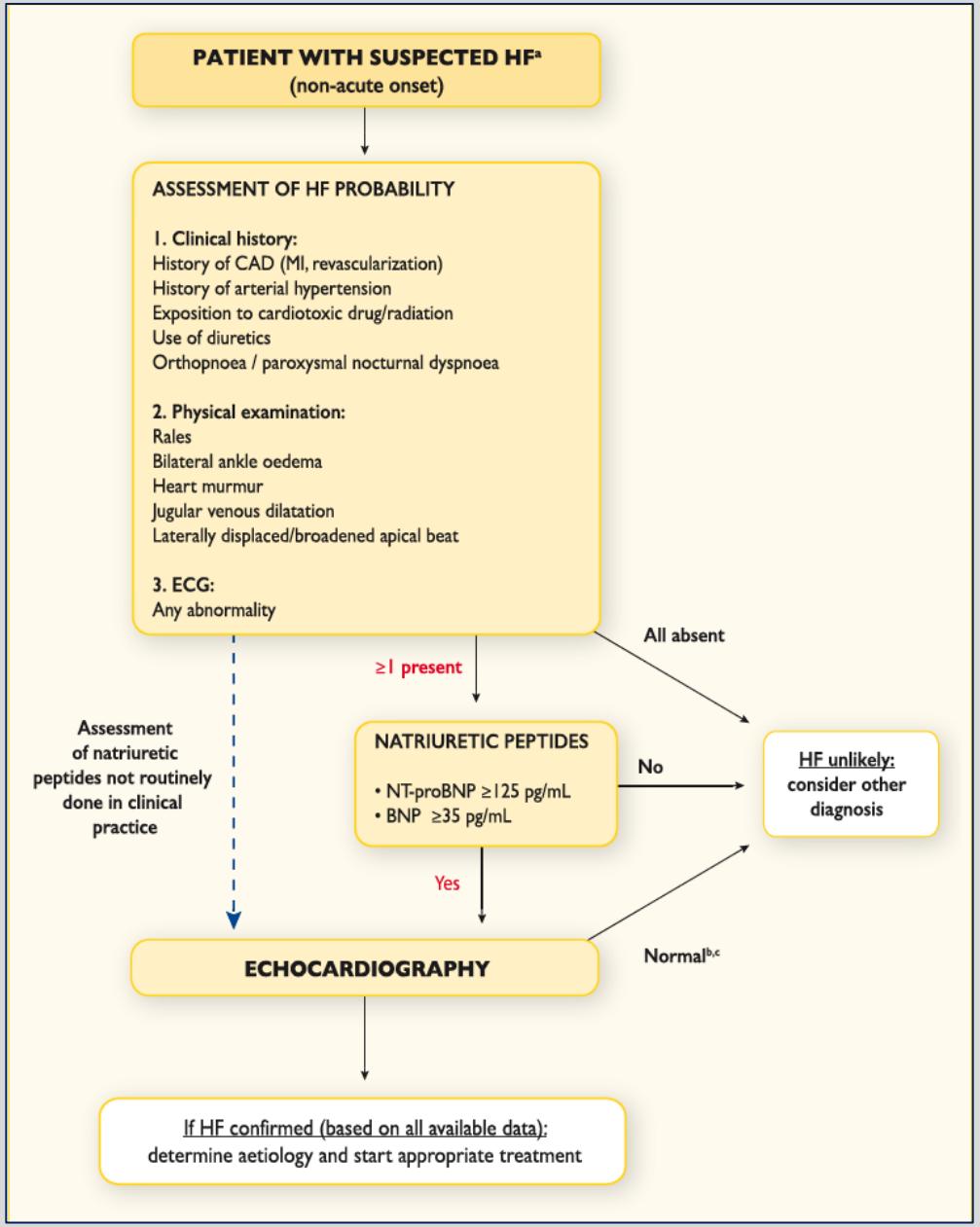
STAGE D: Advanced Heart Failure

Marked HF symptoms that interfere with daily life and with recurrent hospitalizations despite attempts to optimize GDMT

CENTRAL ILLUSTRATION: Noninvasive Assessment of LV Filling Pressure



ESC Guidelines 2016



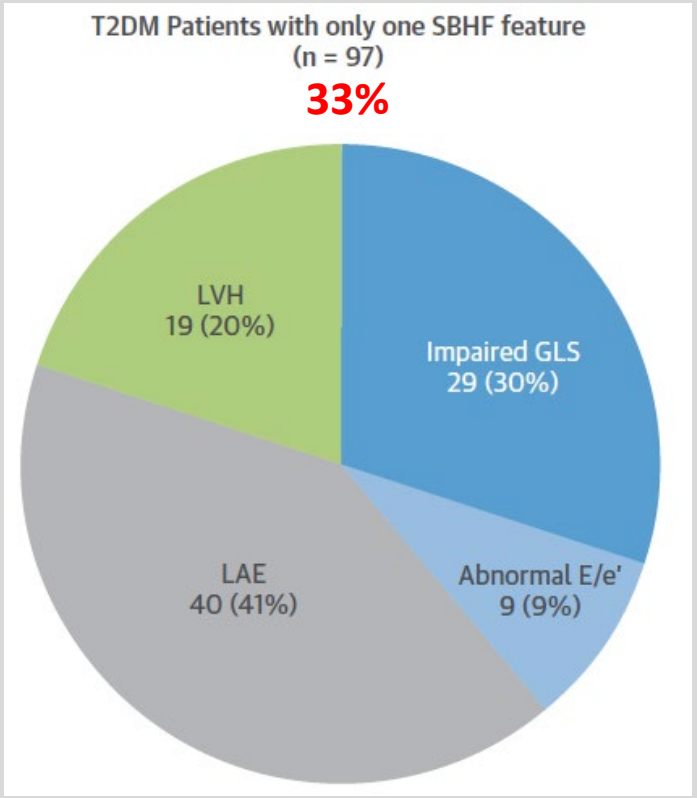
Diagnosis of Nonischemic Stage B Heart Failure in Type 2 Diabetes Mellitus
Optimal Parameters for Prediction of Heart Failure

Wang Y et al *JACC* 2018

TABLE 1 Baseline Clinical and Echocardiographic Characteristics of 290 Elderly Asymptomatic Patients With T2DM (n = 290)

Age, yrs	70.9 ± 4.3
Male	163 (56.2)
Weight, kg	85.9 ± 17.0
Height, cm	168.0 ± 10.3
BMI, kg/m^2	30.3 ± 5.9
Waist circumference, cm	103.4 ± 13.0
HbA_{1c}, mmol/mol	53.7 ± 10.3
Poor HbA_{1c}*	38 (13.1)
Obesity	142 (49.0)

58% !

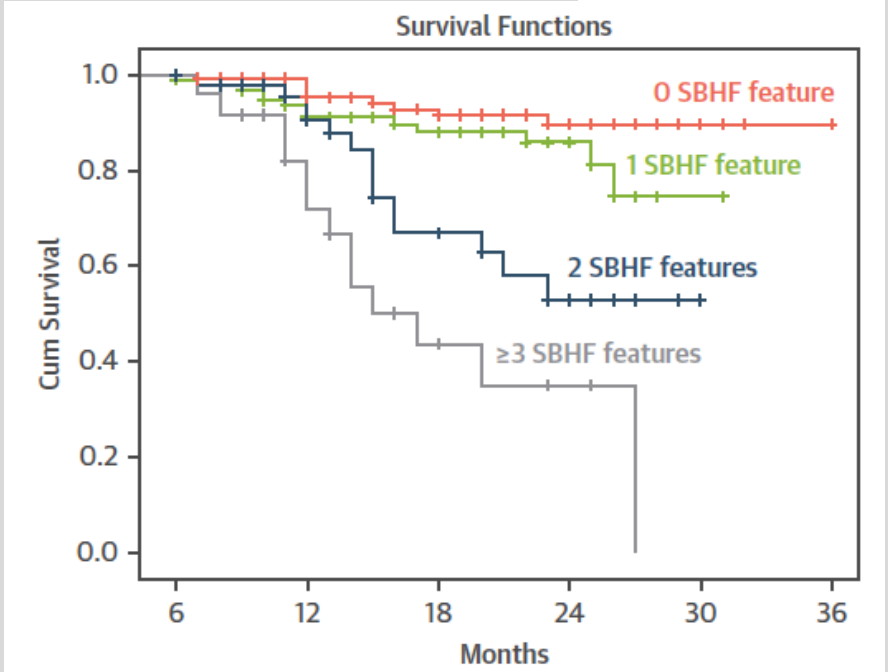


17%
2 features

8%
≥3 features

LVH HR: 2.90; p < 0.001
GLS <16% HR: 2.26; p < 0.008

Incident HF



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- **Cosa fare e non fare una volta che li abbiamo trovati**

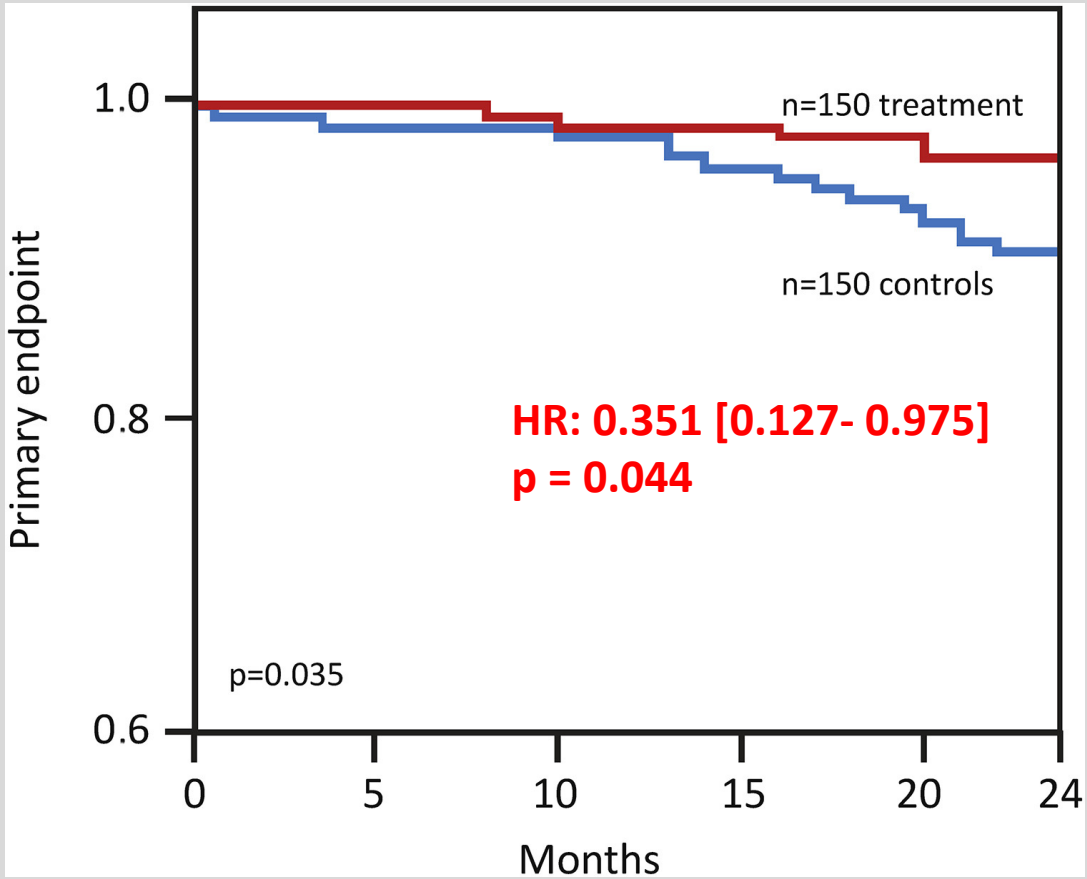
HF Primary prevention study in Stage B HF

PONTIAC STUDY

300 patients with T2D and elevated NT-proBNP (>125 pg/ml) but free of cardiac disease were randomized.

Control group: usual care (Diabetologists)
Intensified group: up-titration of renin-angiotensin system (RAS) antagonists and beta-blockers (Cardiolgists)

hospitalization/death due to cardiac disease



Huelssmann M *et al JACC* 2013

Recommendations for the primary prevention of heart failure in patients with risk factors for its development

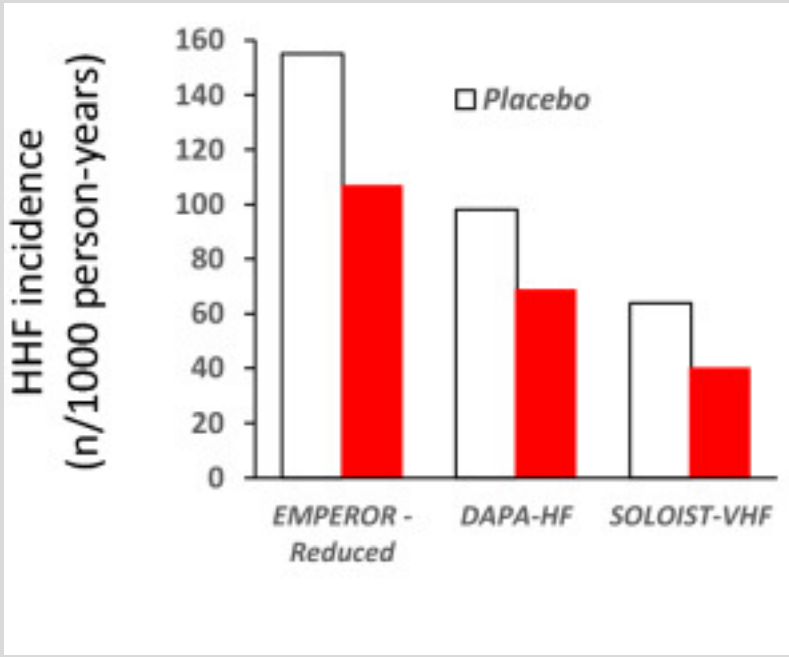
Recommendations	Class	Level
Treatment of hypertension is recommended to prevent or delay the onset of HF, and to prevent HF hospitalizations.	I	A
Treatment with statins is recommended in patients at high risk of CV disease or with CV disease in order to prevent or delay the onset of HF, and to prevent HF hospitalizations.	I	A
SGLT2 inhibitors (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin, sotagliflozin) are recommended in patients with diabetes at high risk of CV disease or with CV disease in order to prevent HF hospitalizations.	I	A
Counselling against sedentary habit, obesity, cigarette smoking, and alcohol abuse is recommended to prevent or delay the onset of HF.	I	C

CV=cardiovascular; HF=heart failure; SGLT2=sodium-glucose co-transporter 2.

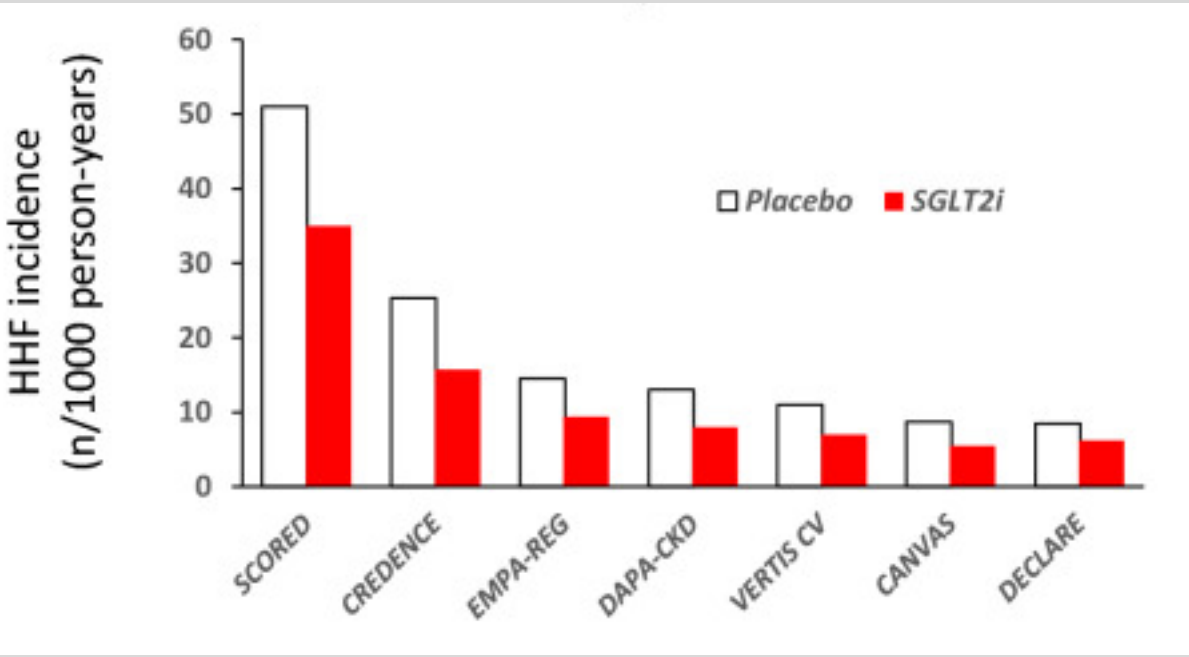
2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab368)

SGLT-2i

Prevenzione secondaria



Prevenzione «primaria»

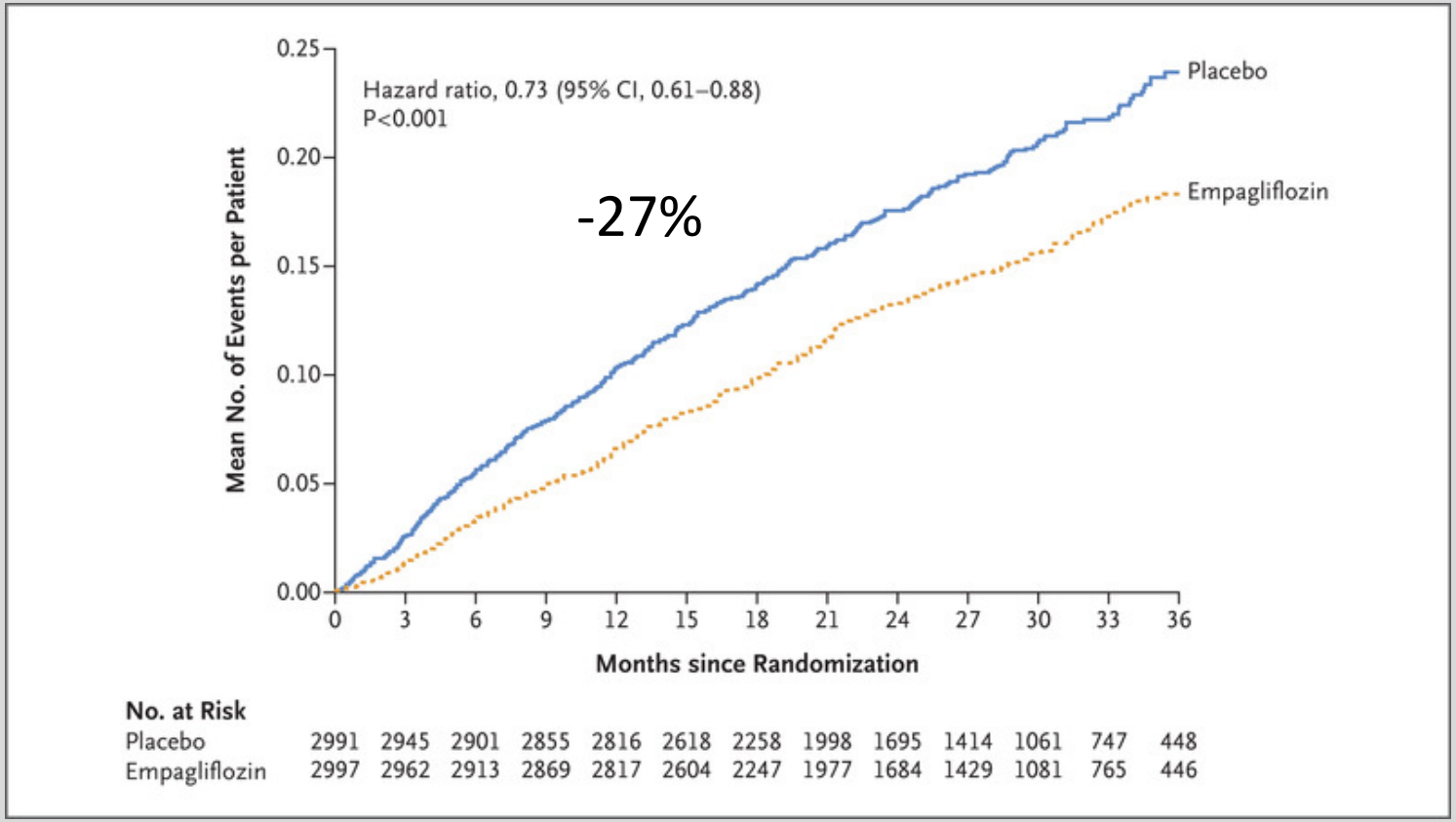


Nauck NA, 2017, Circulation; Natali A et al, 2021, Cardiovasc Diabetol

SGLT-2i anche nell' HFpEF

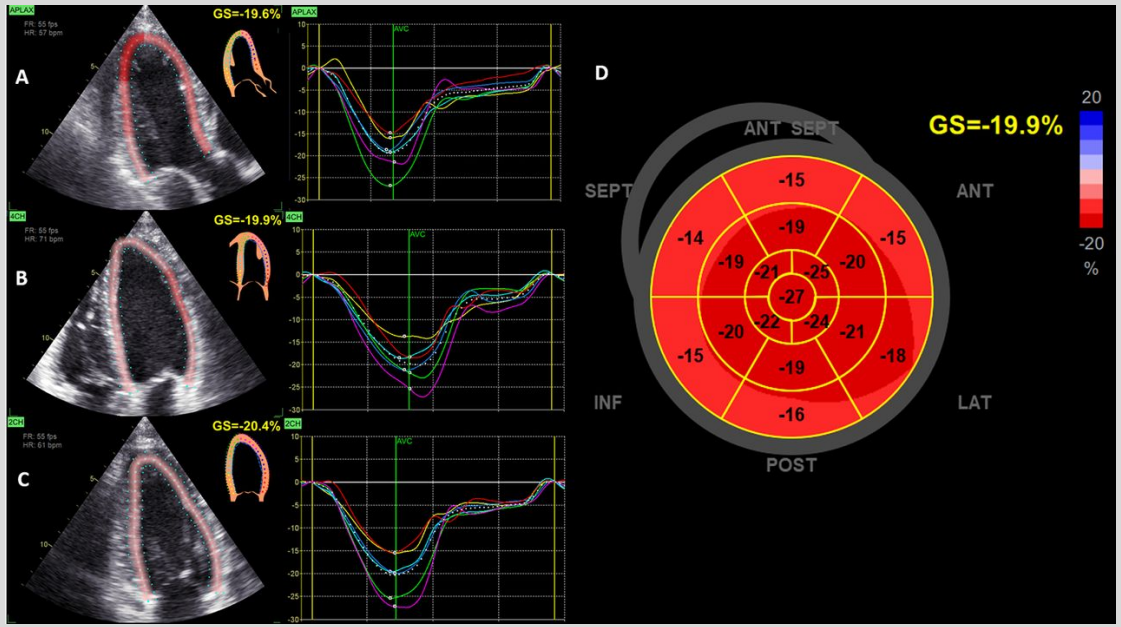
- SGLT2i: unico con impatto prognostico!!

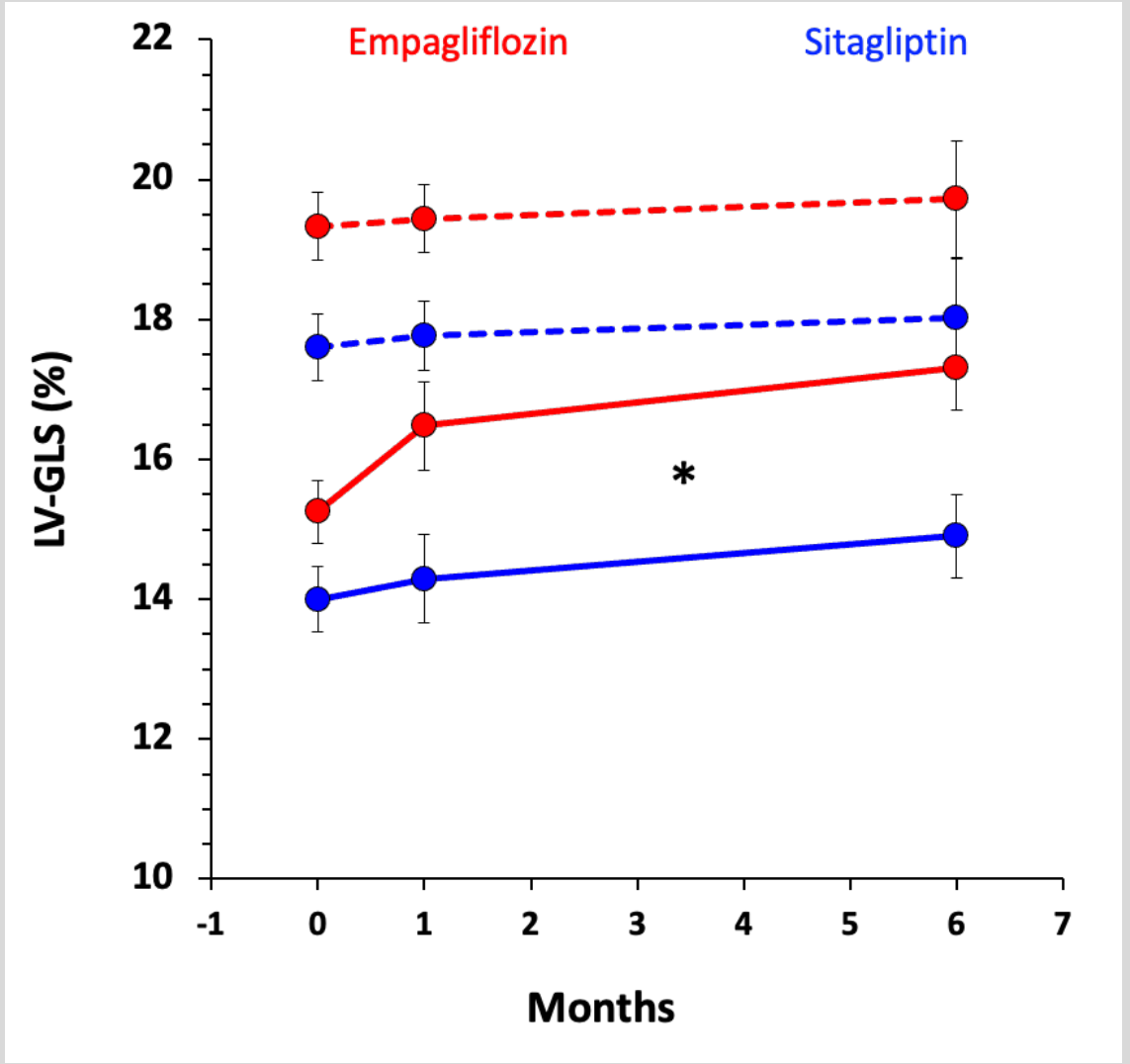
- Spironolattone ?
- Sacubitril+valsartan ?
- Nebivololo ?
- Candesartan ?



«EMPEROR PRESERVED». Anker, 2021, NEJM

SGLT-2i e disfunzione sistolica subclinica

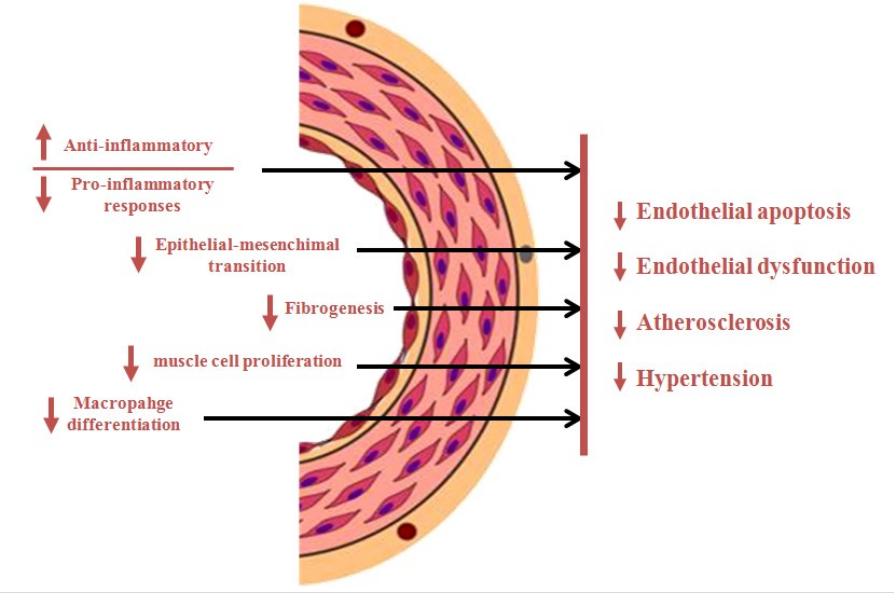


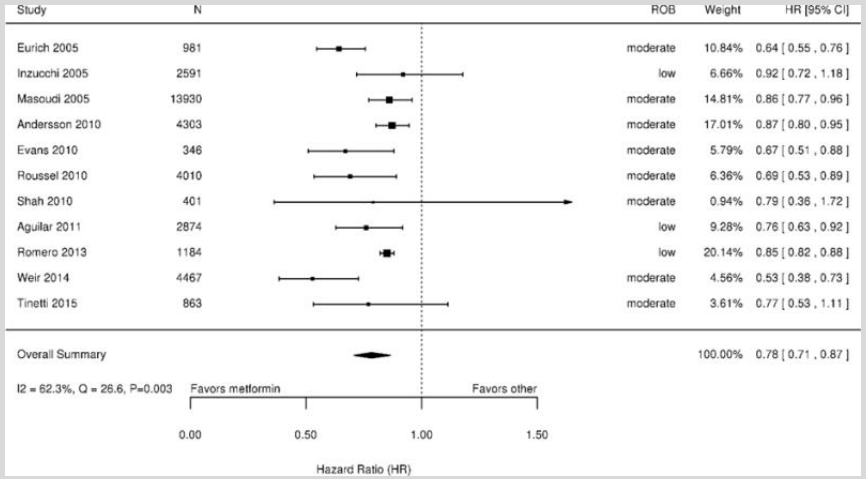


Nesti, 2022, Cardiovasc Diabetol

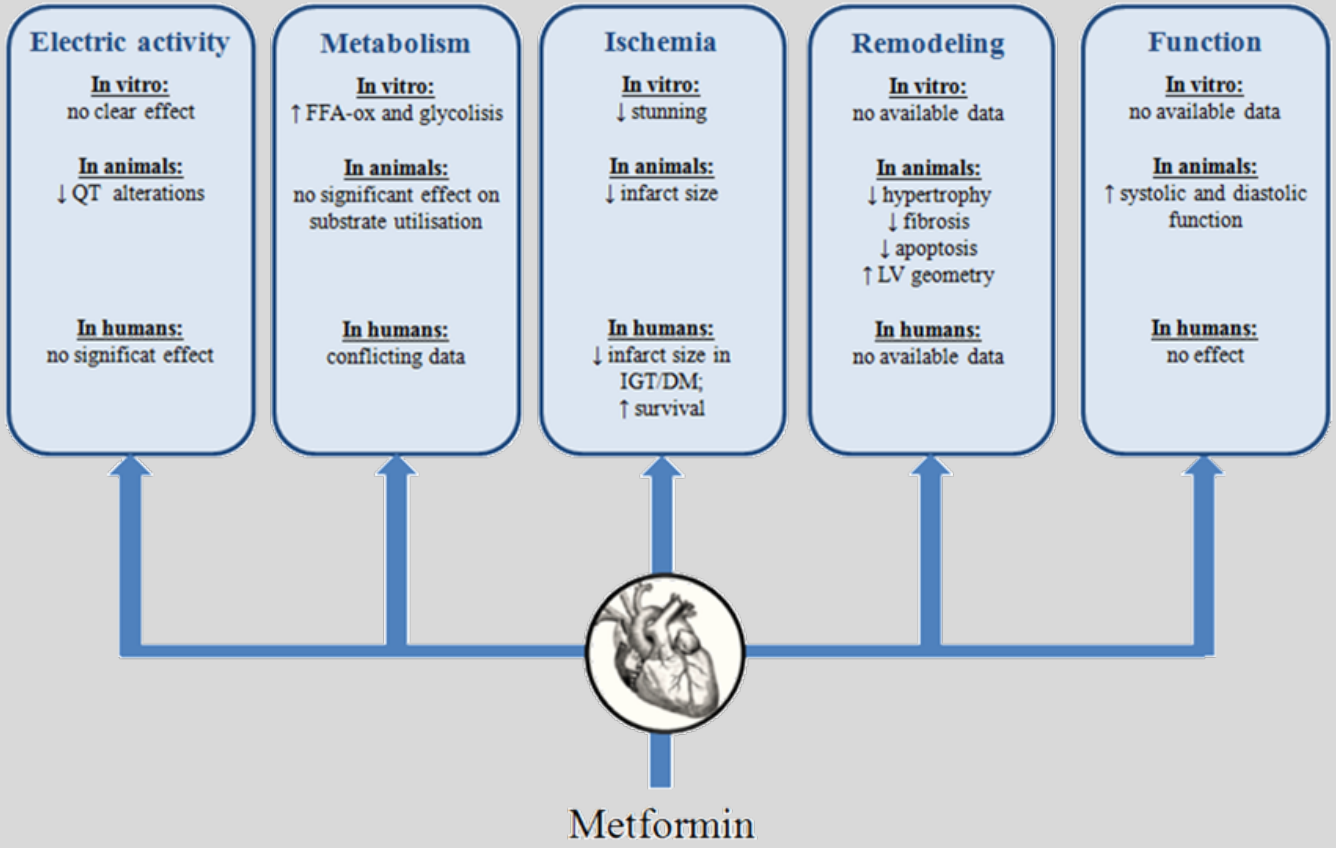
Grazie per l’attenzione

Metformina





No RCT in HF + T2D



In 2006 FDA removed absolute HF contraindication

Still first choice

Nesti L et al, 2017, NMCD; Crowley MJ, 2017, Ann Intern Med

Pioglitazone

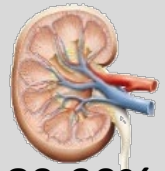
NO in HF (NYHA II-IV)

CAUTELA nei soggetti a rischio di HF

Da evitare associazione con insulina

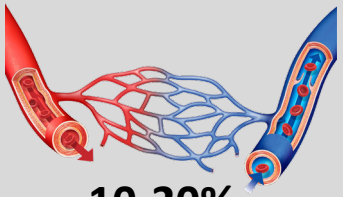
Edema 4-7% (x3 vs placebo)

Sinergico con insulina (+20%)



80-90%

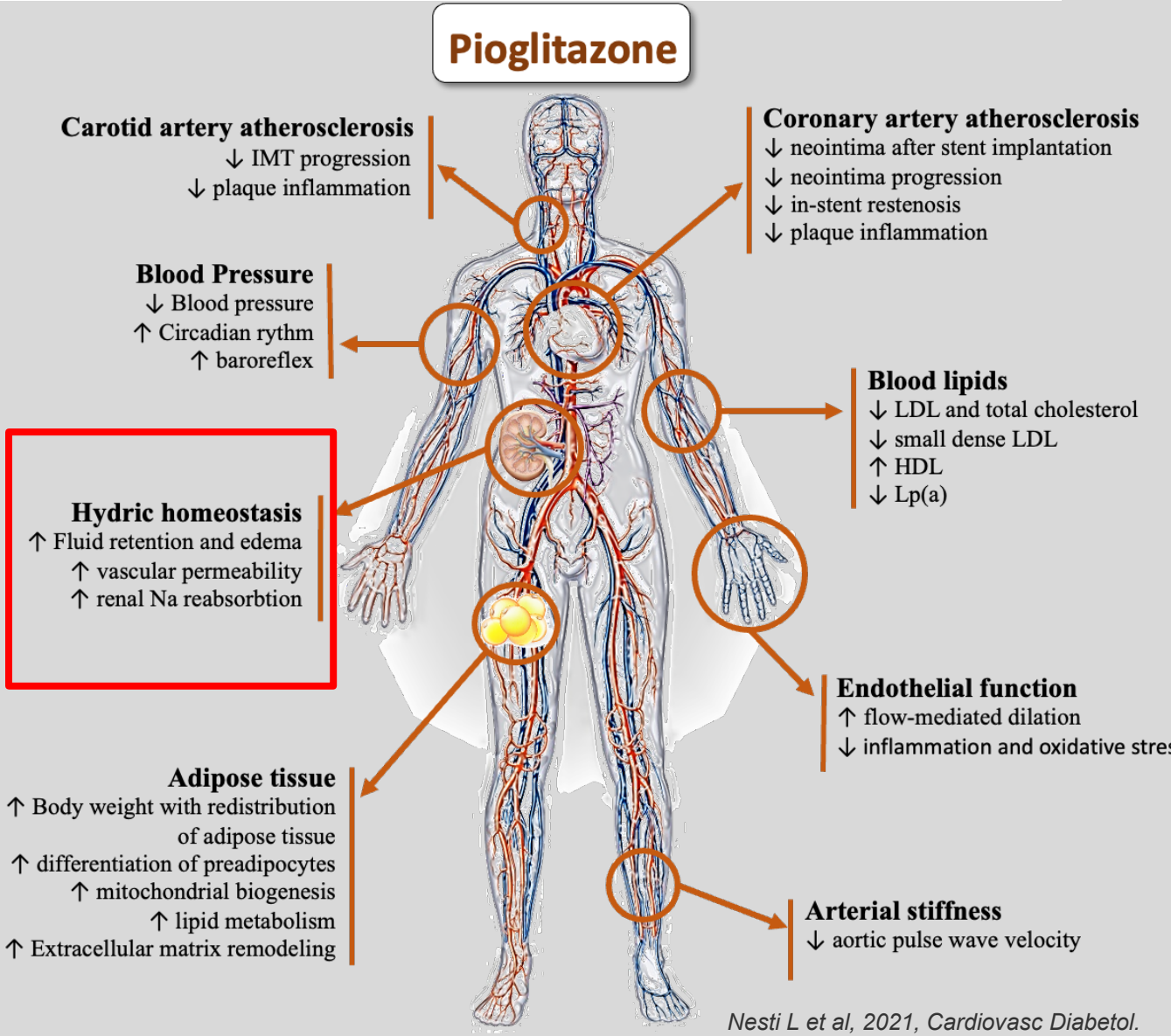
↓ NH3
↓ AQP
↓ ENaC ?



10-20%

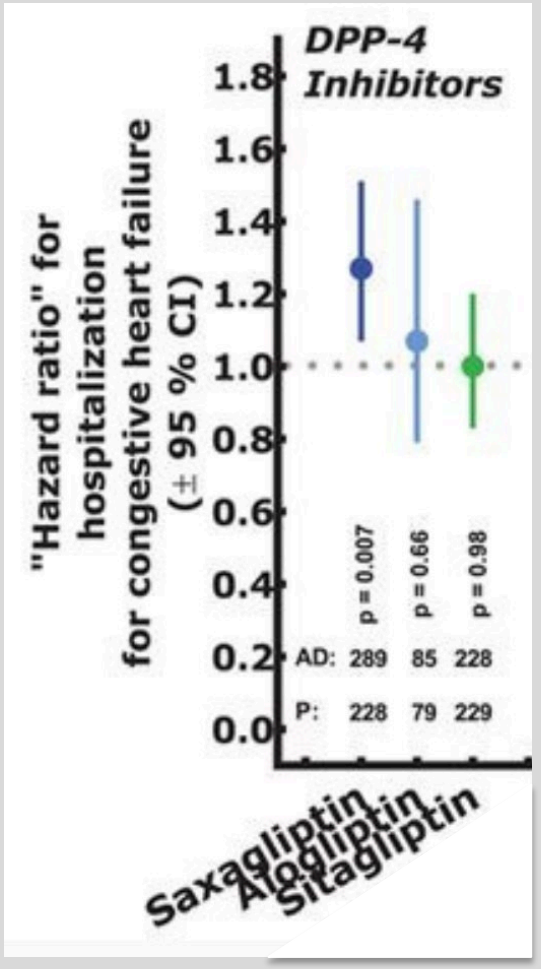
↑ VEGF

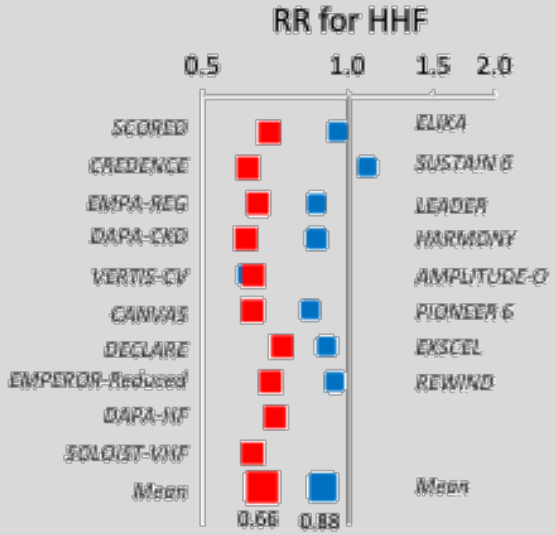
↓ L-type Ca channel

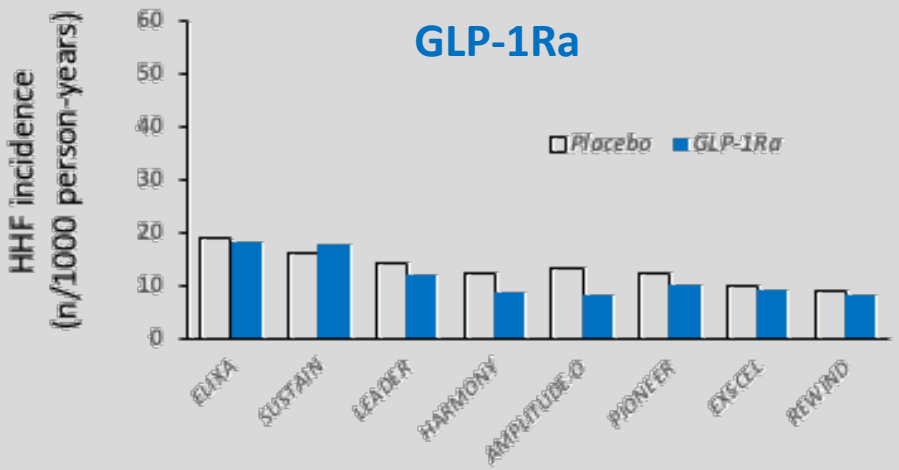


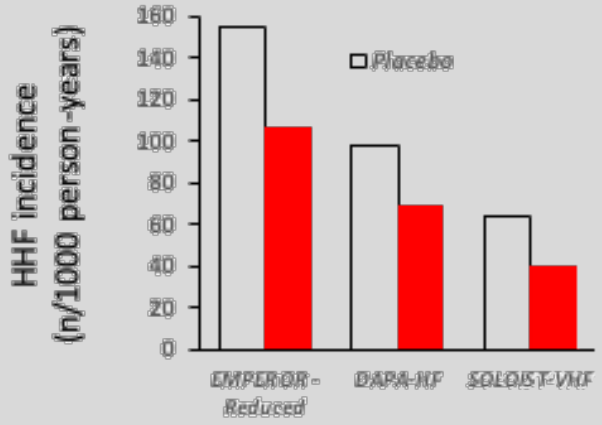
Nesti L et al, 2021, Cardiovasc Diabetol.

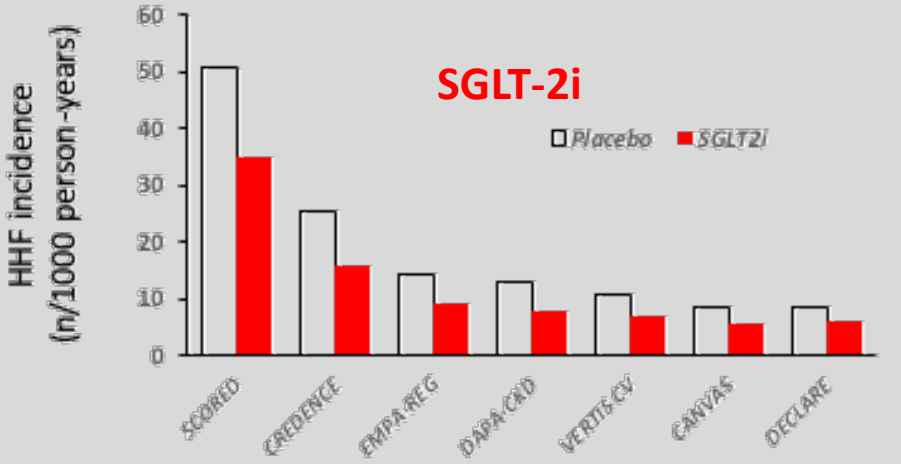
DPP-4i, GLP-1Ra, SGLT-2i











Nauck NA, 2017, Circulation; Natali A et al, 2021, Cardiovasc Diabetol