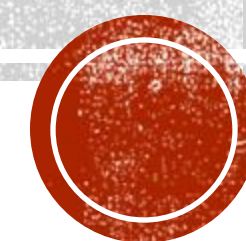


**IL CASO DELLE PATOLOGIE CARDIOMETABOLICHE —
DAI MODELLI PRESTAZIONALI ALLA PRESA IN
CARICO DEL PAZIENTE**

Dott. Massimo Milli
Direttore SOC Cardiologia Firenze 1
massimo.milli@uslcentro.toscana.it



AGENDA

Terapia dell'ipercolesterolemia: potenzialità e real word

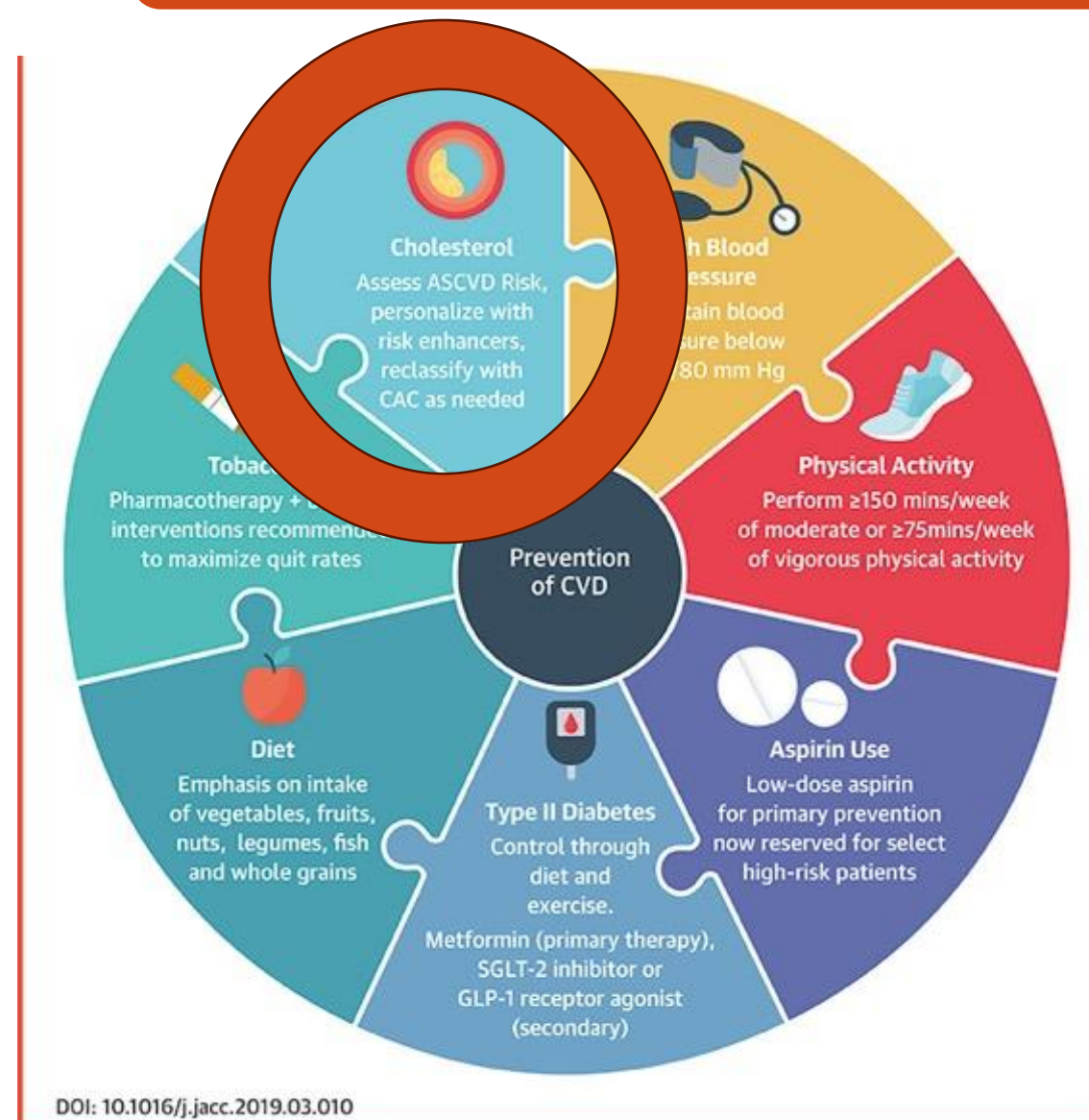
Nuove indicazioni dalle LG per l'ipertensione arteriosa

Diabete mellito & co

Riflessioni e proposte gestionali



Ruolo del colesterolo LDL



Il colesterolo viene, ad oggi, universalmente considerato non un semplice fattore di rischio ma, un **fattore causale di malattia aterosclerotica**



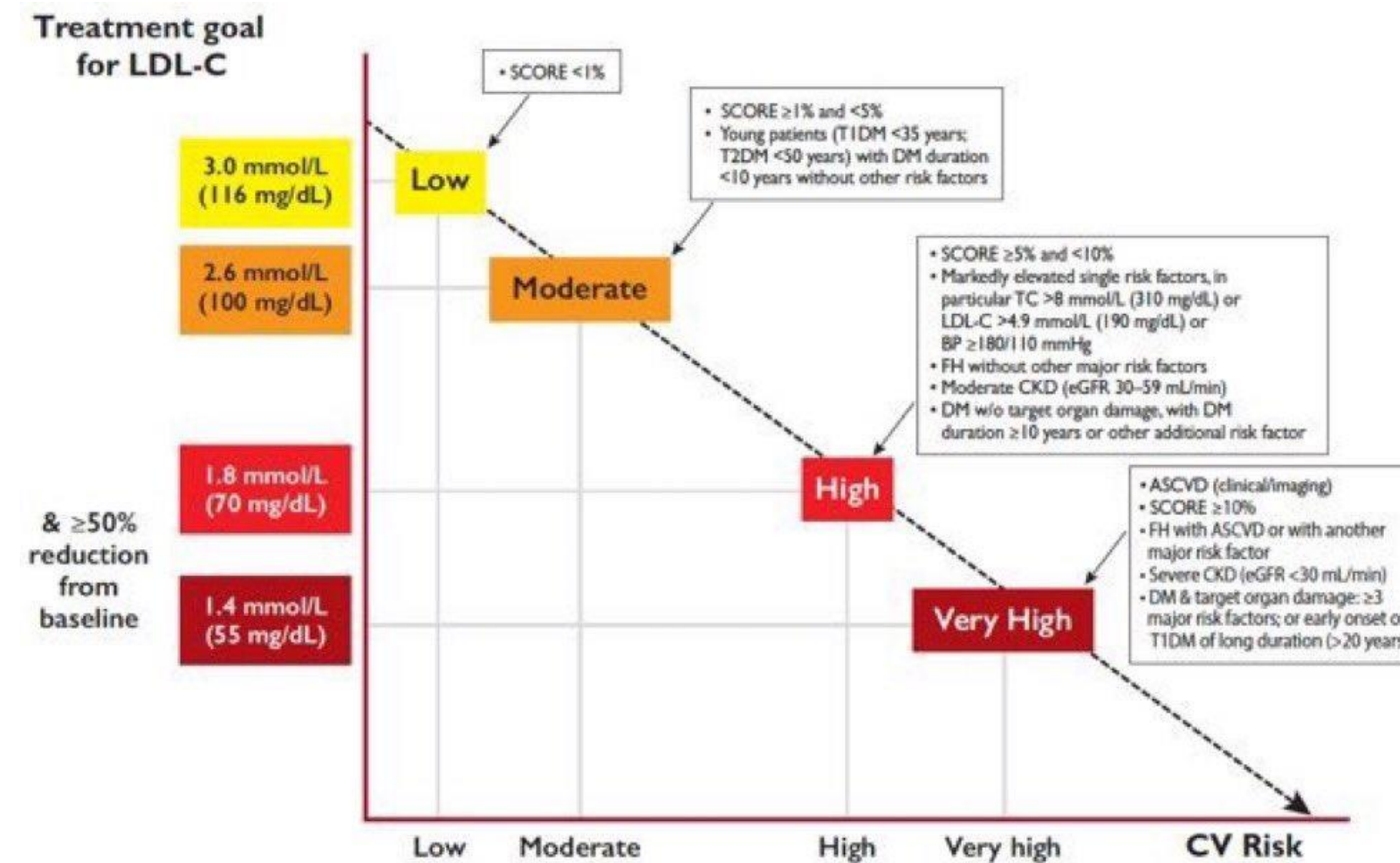
ESC Congress 2019

LDL-C: The race to the bottom

“LDL-C it's a principal risk factor (cause) of a series cardiovascular disease. We know that there are other extremely important risk factors we know about **blood pressure, cigarette smoking, diabetes, inflammation**, but in the experimental models in the absence of LDL-C is virtually impossible to produce a plaque”



TARGET DIVERSI PER PAZIENTI DIVERSI

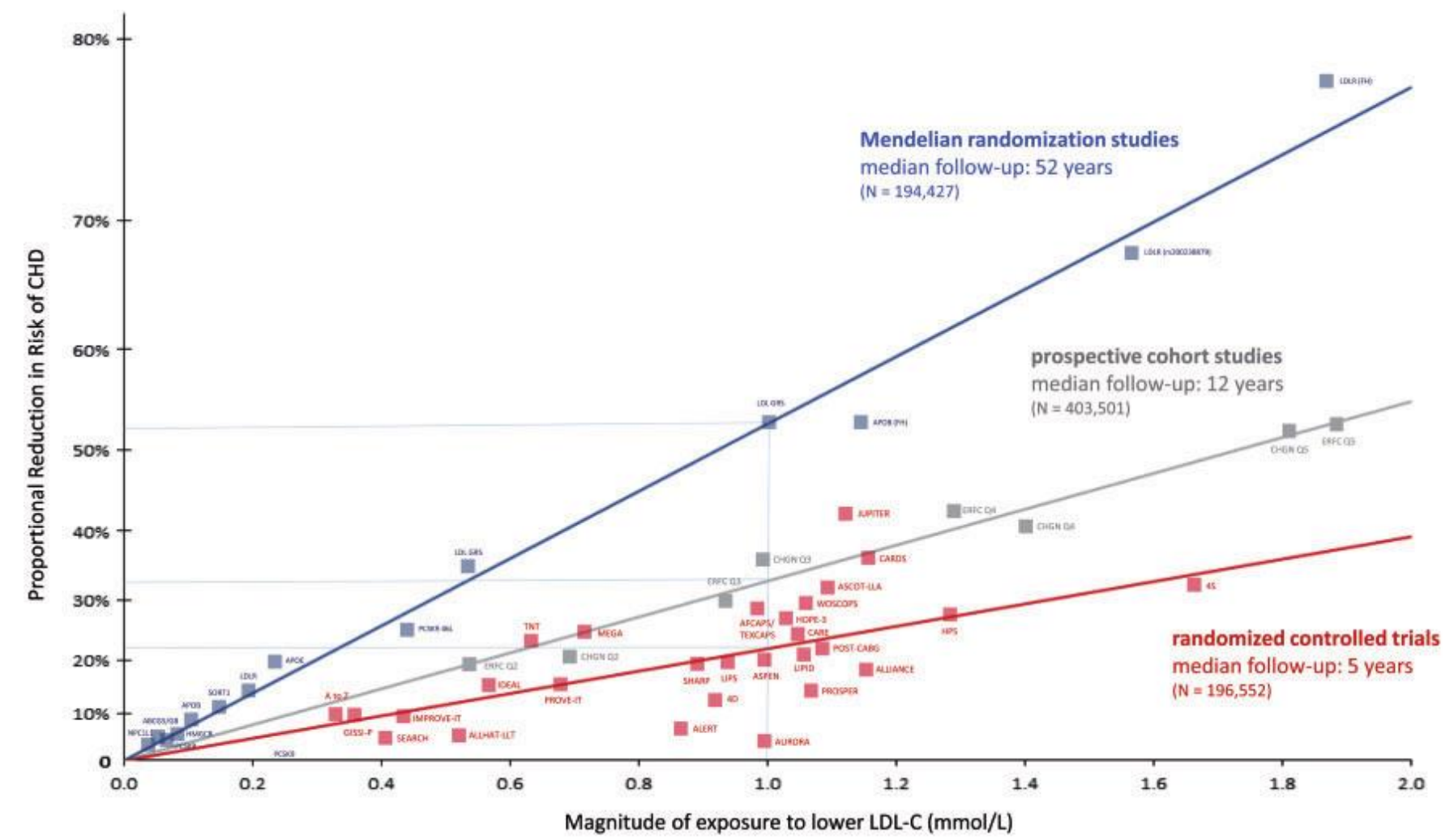


ESC guidelines 2019

ESC European Society of Cardology
 European Heart Journal (2017) 38, 2459-2472
 CURRENT OPINION

Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel

Più tempo siamo esposti a bassi valori di colesterolo minore sarà il nostro rischio di presentare un evento aterosclerotico





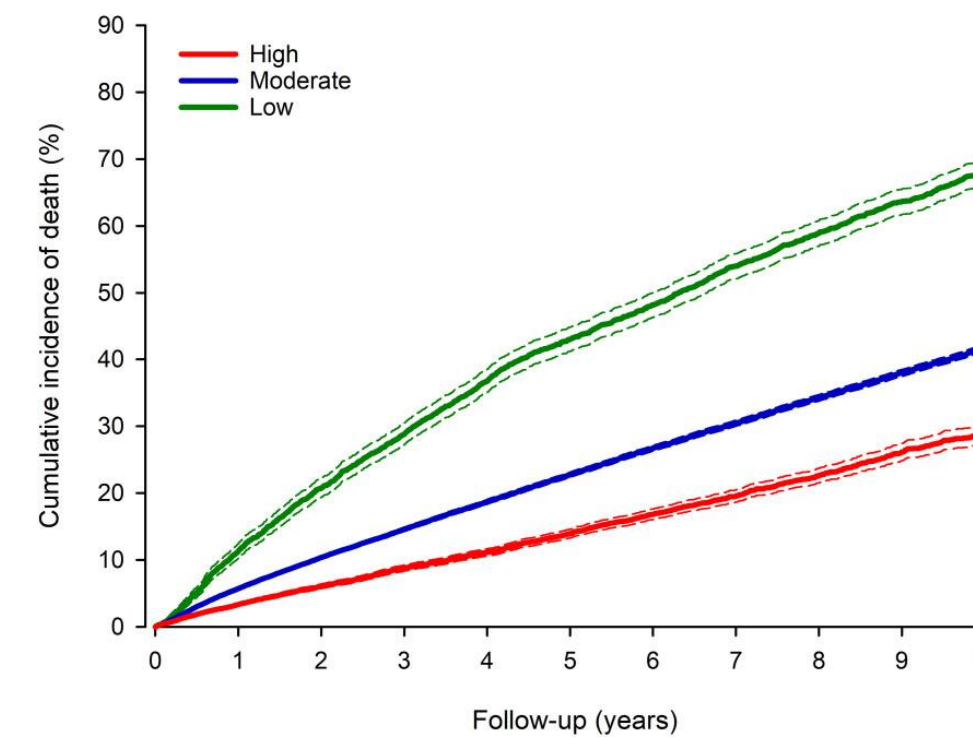
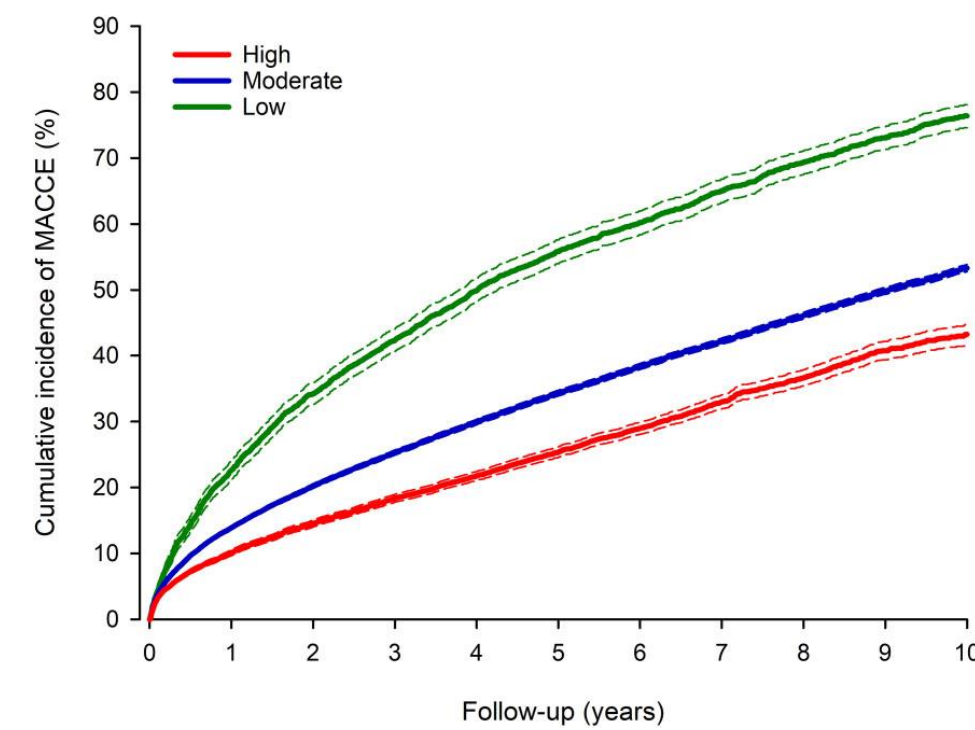
ESC
 European Society of Cardiology
 European Heart Journal - Cardiovascular Pharmacotherapy (2023) 9, 156–164
<https://doi.org/10.1093/ehjcvp/pvac064>

ORIGINAL ARTICLE
 Acute Coronary Syndromes

Initial statin dose after myocardial infarction and long-term cardiovascular outcomes

Ville Kytö^{1,2,*}, Päivi Rautava^{2,3} and Aleksi Törnio^{4,5}

INIZIARE PRESTO

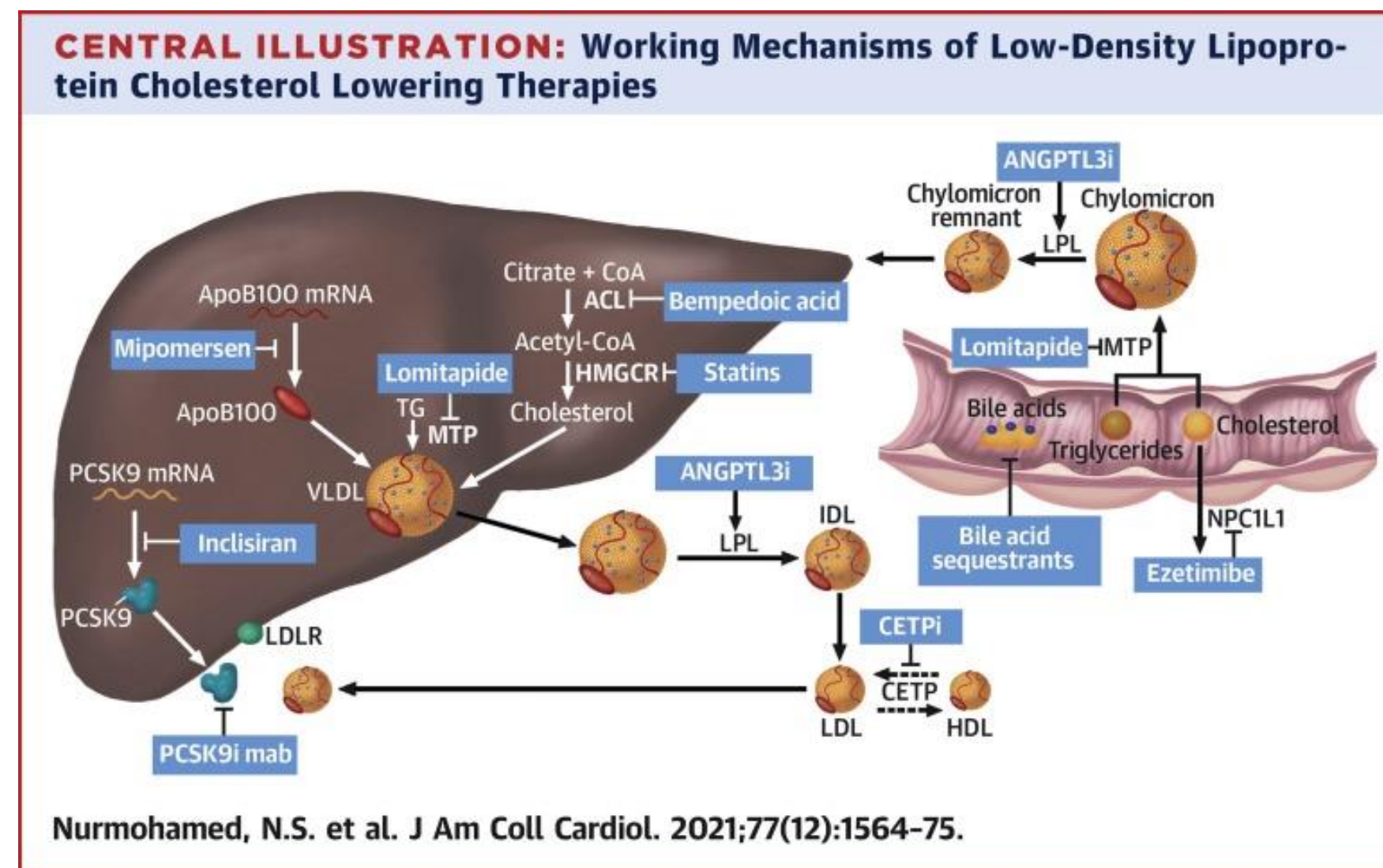


Conclusion

Higher initial statin dose after MI is dose-dependently associated with better long-term cardiovascular outcomes. These results underline the importance of using a high statin dose early after MI.



TERAPIE A DISPOSIZIONE



LA 'POTENZA' DEI FARMACI A DISPOSIZIONE

Farmaco	Riduzione attesa di C-LDL
Statina a moderata intensità	~30%
Statina ad alta intensità	~50%
Ezetimibe	~18% in monoterapia ~65% in aggiunta a statine ad alta intensità
Anticorpi monoclonali anti- PCSK9 Inclisiran	~60% in monoterapia ~75% in associazione a statine ad alta intensità ~85% in associazione a statine ad alta intensità ed ezetimibe
Acido bempedoico	~18% in aggiunta a statine (intensità moderata o alta) ~24% in monoterapia ipolipemizzante ~25% in pazienti intolleranti alle statine (± ezetimibe) ~30% in aggiunta ad anticorpi monoclonali anti-PCSK9* ~38% in combinazione a dose fissa con ezetimibe (± statine) ~60% in combinazione con ezetimibe e atorvastatina 20 mg

PCSK9, proproteina della convertasi subtilisina/kexina di tipo 9.
 *Testato con evolocumab.

G Ital Cardiol 2023;24(6):490-498



CONCLUSIONI

Cholesterol lowering trials in coronary heart disease:
frequency of citation and outcome.

[U. Ravnskov](#)

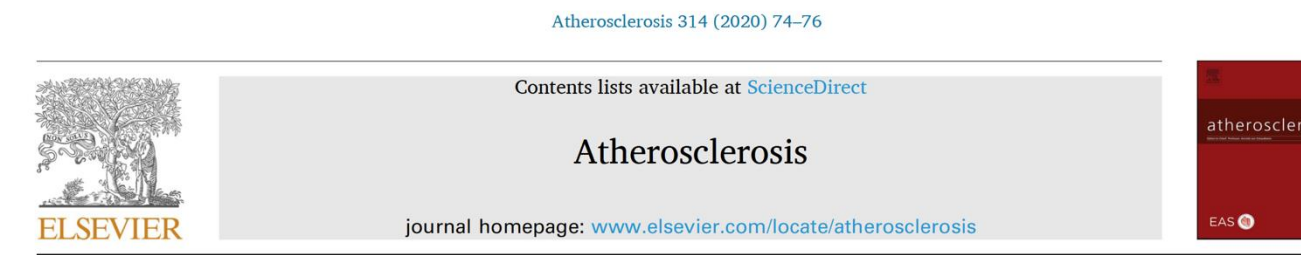
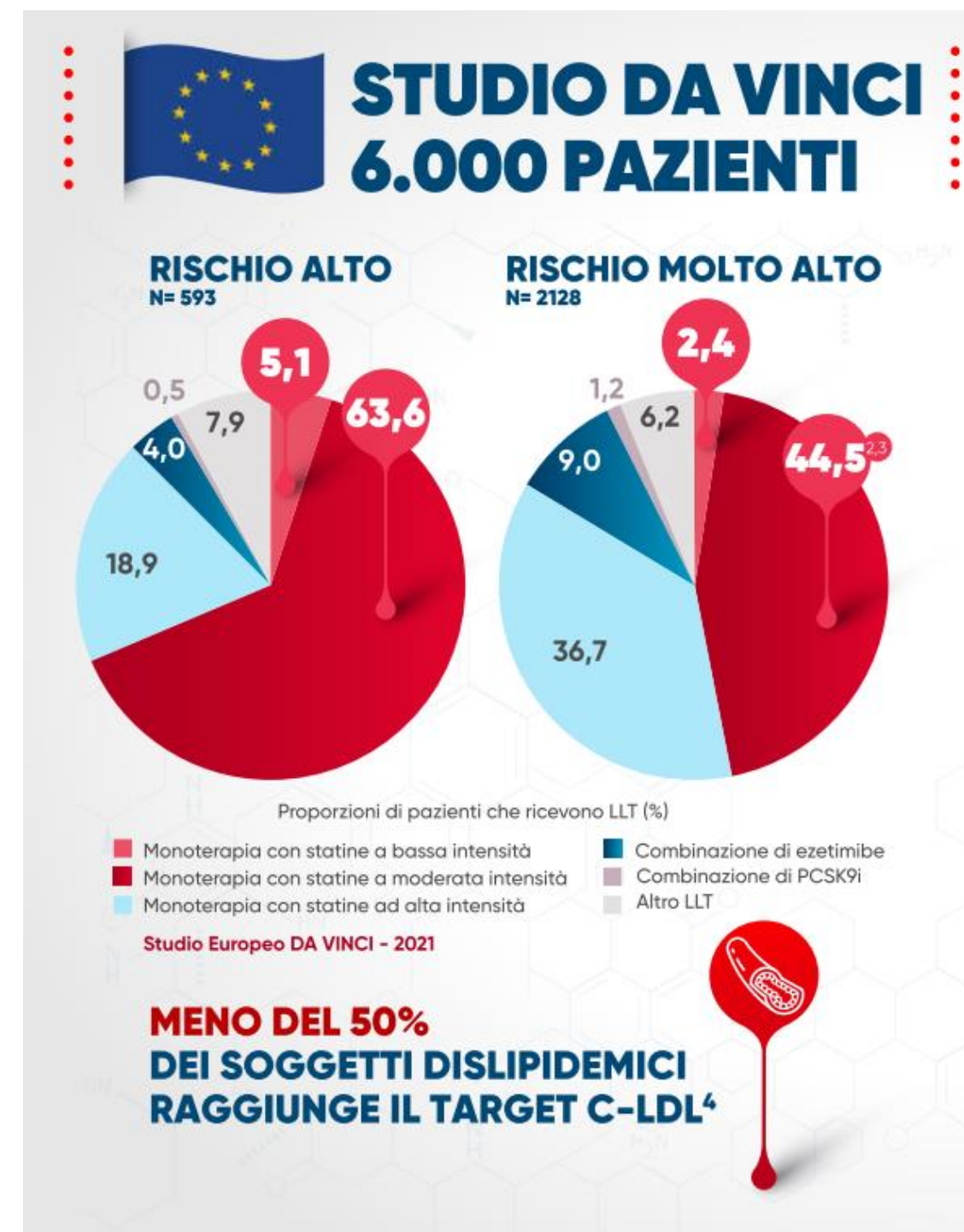
Conclusion—Lowering serum cholesterol concentrations does not reduce mortality and is unlikely to prevent coronary heart disease. Claims of the opposite are based on preferential citation of supportive trials.

BMJ. 1992 Jul 4; 305(6844): 15–19



- LOWER
- SOONER
- FOR LONGER
- EFFICACY
- PERSISTENCE
- SAFETY





EAS Updates

DA VINCI study: Change in approach to cholesterol management will be needed to reduce the implementation gap between guidelines and clinical practice in Europe

Jane K. Stock

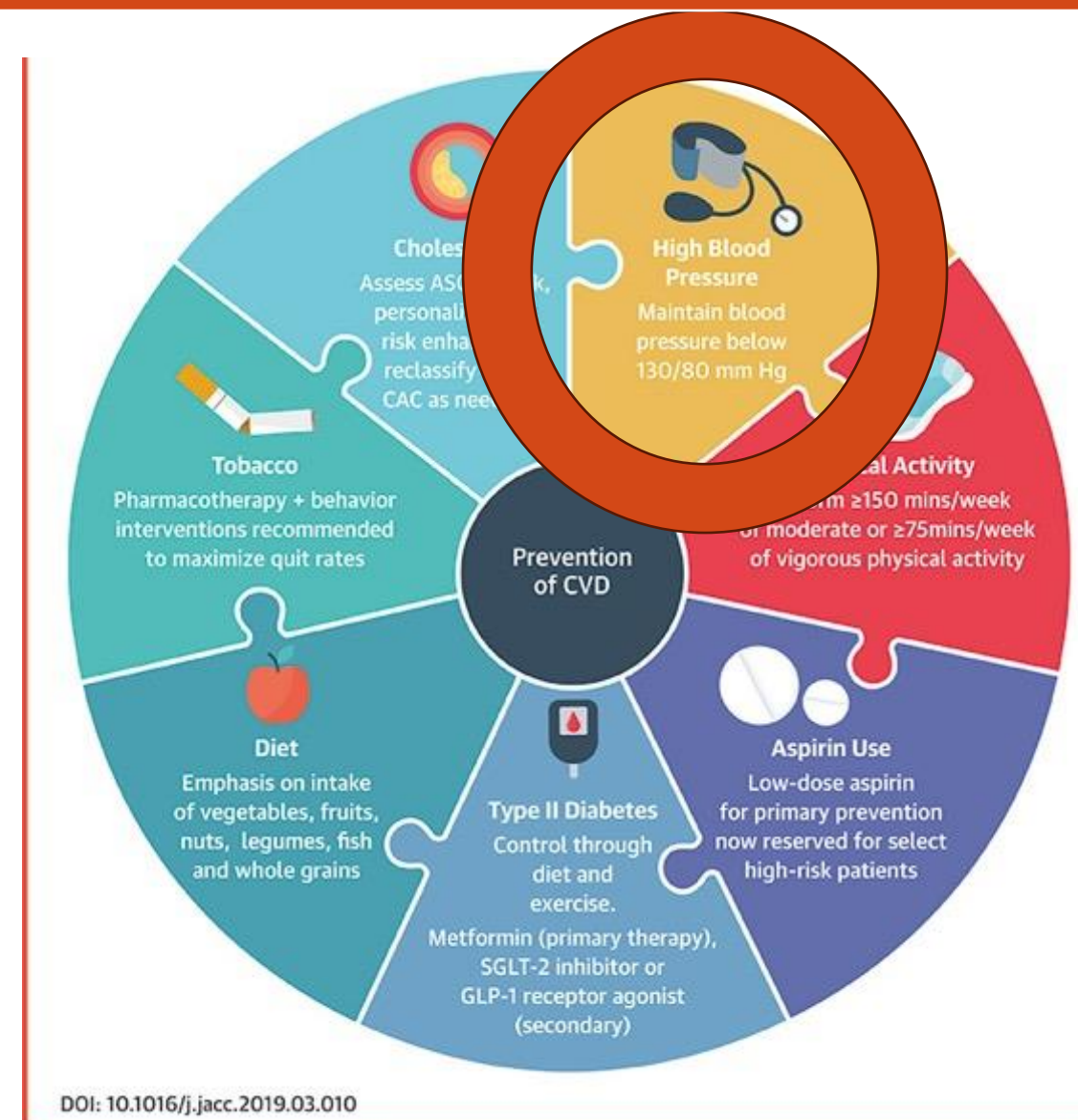
MENO del 10%
 dei pazienti a RISCHIO CV ELEVATO o MOLTO ELEVATO riceve una **combinazione di statina ed ezetimibe**¹

7 SU 10
 dei pazienti a RISCHIO CV ELEVATO sono ancora trattati con **statine a bassa e media intensità**¹

Jane K Stock Atherosclerosis 2020



Il paziente con ipertensione arteriosa



ESC
 European Society of Cardiology
 European Heart Journal (2024) 00, 1–107
<https://doi.org/10.1093/eurheartj/ehae178>

ESC GUIDELINES

2024 ESC Guidelines for the management of elevated blood pressure and hypertension

Developed by the task force on the management of elevated blood pressure and hypertension of the European Society of Cardiology (ESC) and endorsed by the European Society of Endocrinology (ESE) and the European Stroke Organisation (ESO)

Cosa c'è di nuovo?

NUOVA CLASSIFICAZIONE

Non-elevated blood pressure	Elevated blood pressure	Hypertension
<p>Office BP</p> <p>SBP <120 mmHg and DBP <70 mmHg</p>	<p>Office BP</p> <p>SBP 120–139 mmHg or DBP 70–89 mmHg</p>	<p>Office BP</p> <p>SBP ≥140 mmHg or DBP ≥90 mmHg</p>
<p>HBPM</p> <p>SBP <120 mmHg and DBP <70 mmHg</p>	<p>HBPM</p> <p>SBP 120–134 mmHg or DBP 70–84 mmHg</p>	<p>HBPM</p> <p>SBP ≥135 mmHg or DBP ≥85 mmHg</p>
<p>ABPM</p> <p>Daytime SBP <120 mmHg and Daytime DBP <70 mmHg</p>	<p>ABPM</p> <p>Daytime SBP 120–134 mmHg or Daytime DBP 70–84 mmHg</p>	<p>ABPM</p> <p>Daytime SBP ≥135 mmHg or Daytime DBP ≥85 mmHg</p>
<p>Insufficient evidence confirming the efficacy and safety of BP pharmacological treatment</p>	<p>Risk stratify to identify individuals with high cardiovascular risk for BP pharmacological treatment</p>	<p>Cardiovascular risk is sufficiently high to merit BP pharmacological treatment initiation</p>



TARGET PIÙ AMBIZIONI

To reduce CVD risk, it is recommended that treated systolic BP values in most adults be targeted to 120–129 mmHg, provided the treatment is well tolerated.

I **A**

PAS 120-129 mmHg

In cases where on-treatment systolic BP is at or below target (120–129 mmHg) but diastolic BP is not at target (≥ 80 mmHg), intensifying BP-lowering treatment to achieve an on-treatment diastolic BP of 70–79 mmHg may be considered to reduce CVD risk.

IIb **C**

PAD 70-79 mmHg

Because the CVD benefit of an on-treatment systolic BP target of 120–129 mmHg may not generalize to the following specific settings, personalized and more lenient systolic BP targets (e.g. < 140 mmHg): should be considered among patients meeting the following criteria:

IIa **C**

- pre-treatment, symptomatic, orthostatic hypotension;
- and/or age ≥ 85 years.

Because the CVD benefit of an on-treatment systolic BP target of 120–129 mmHg may not generalize to the following specific settings, personalized and more lenient BP targets (e.g. $< 140/90$ mmHg) may be considered among patients meeting the following criteria:

IIb **C**

- clinically significant, moderate to severe frailty at any age;
- and/or limited predicted lifespan (< 3 years).



Epidemiology/Population Science

May Measurement Month 2019
 The Global Blood Pressure Screening Campaign of the International Society of Hypertension

A che punto siamo?

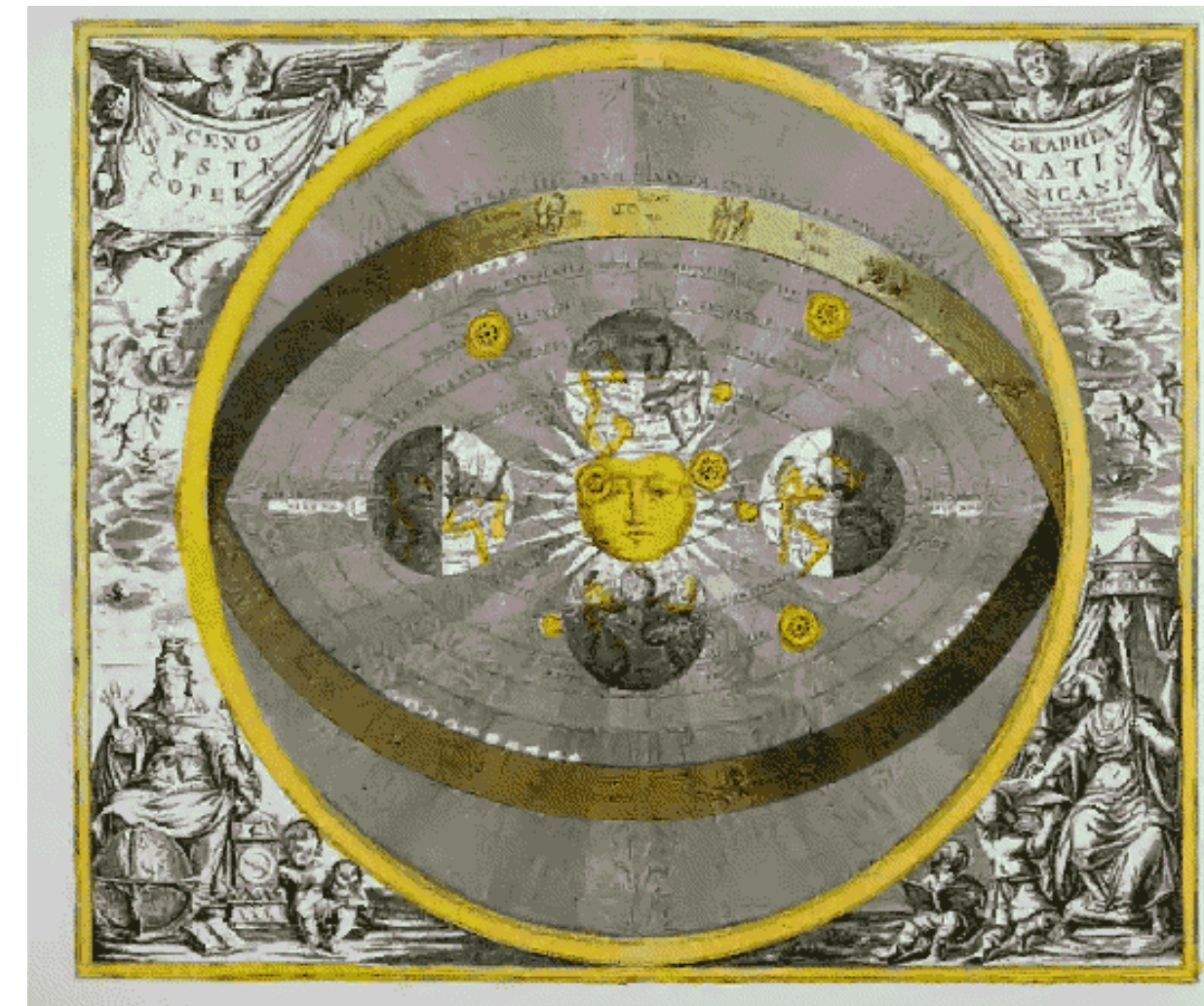
Sottoposti a screening 1 508 130

Region	Number With Hypertension	Proportion With Hypertension	Proportion of Hypertensives Aware	Proportion of Hypertensives on Medication	Proportion of Those on Medication With Controlled BP	Proportion of All Hypertensives Controlled
South Asia	138 236	29.3%	46.2%	43.1%	55.6%	23.9%
East Asia	86 020	30.6%	57.9%	54.7%	63.1%	34.5%
Americas	107 752	41.2%	73.0%	69.7%	61.2%	42.6%
Sub-Saharan Africa	49 616	27.9%	42.7%	34.5%	49.3%	17.0%
South-east Asia and Australasia	58 156	47.8%	65.5%	62.8%	59.6%	37.4%
Europe	46 881	43.6%	71.5%	64.4%	47.9%	30.8%
Northern Africa and Middle East	26 677	30.6%	61.6%	58.1%	58.9%	34.2%
Worldwide	513 337	34.0%	58.7%	54.7%	57.8%	31.7%

DOI: 10.1161/HYPERTENSIONAHA.120.14874

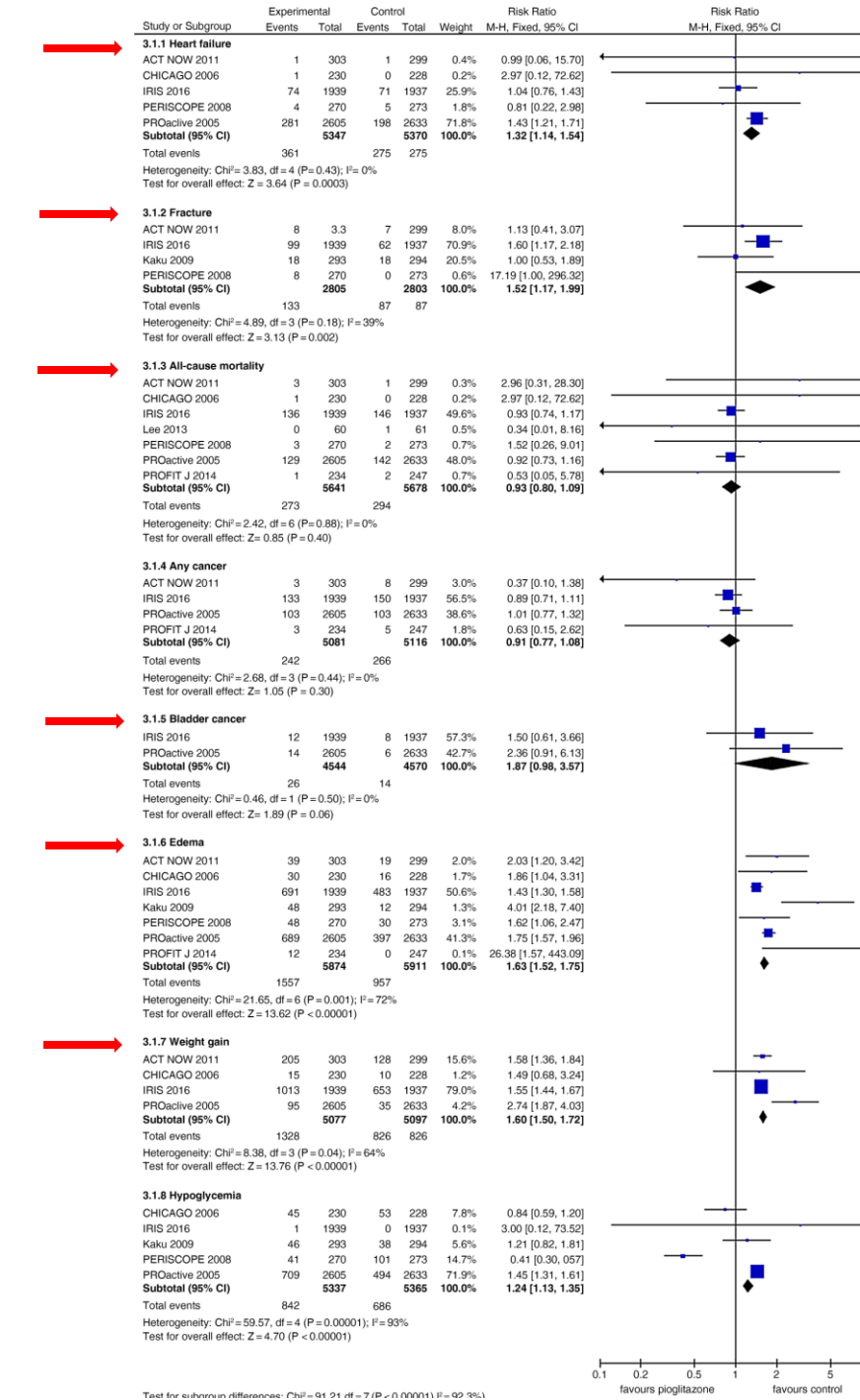
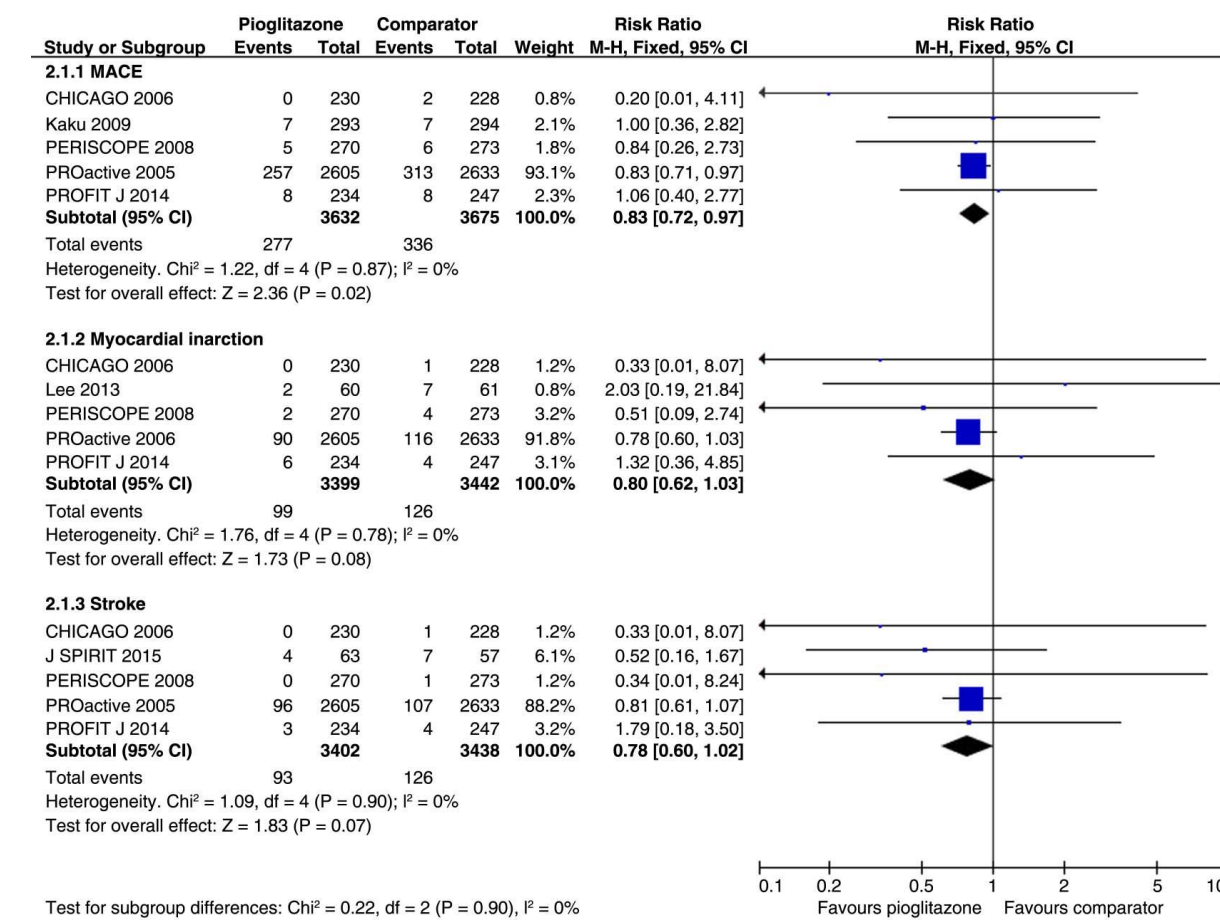


Diabete mellito & co

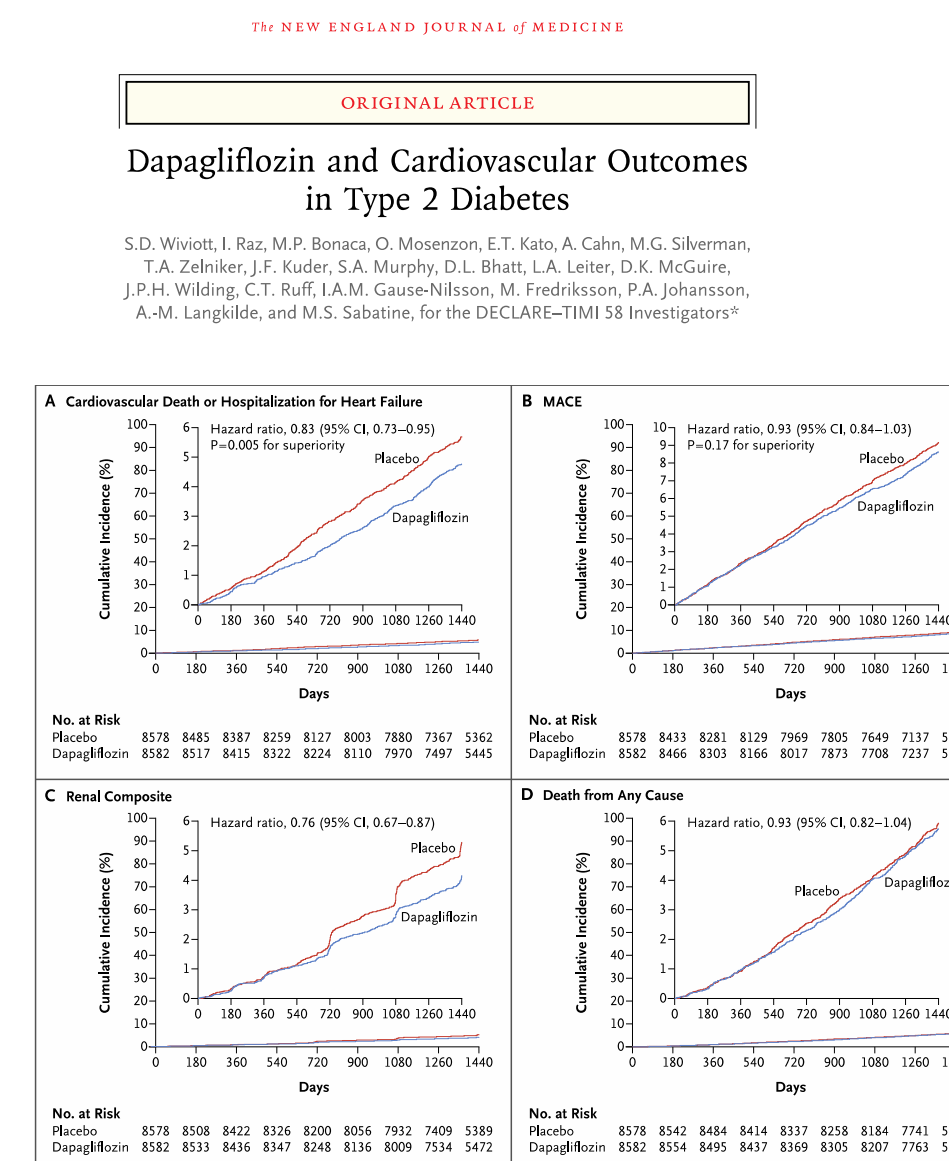
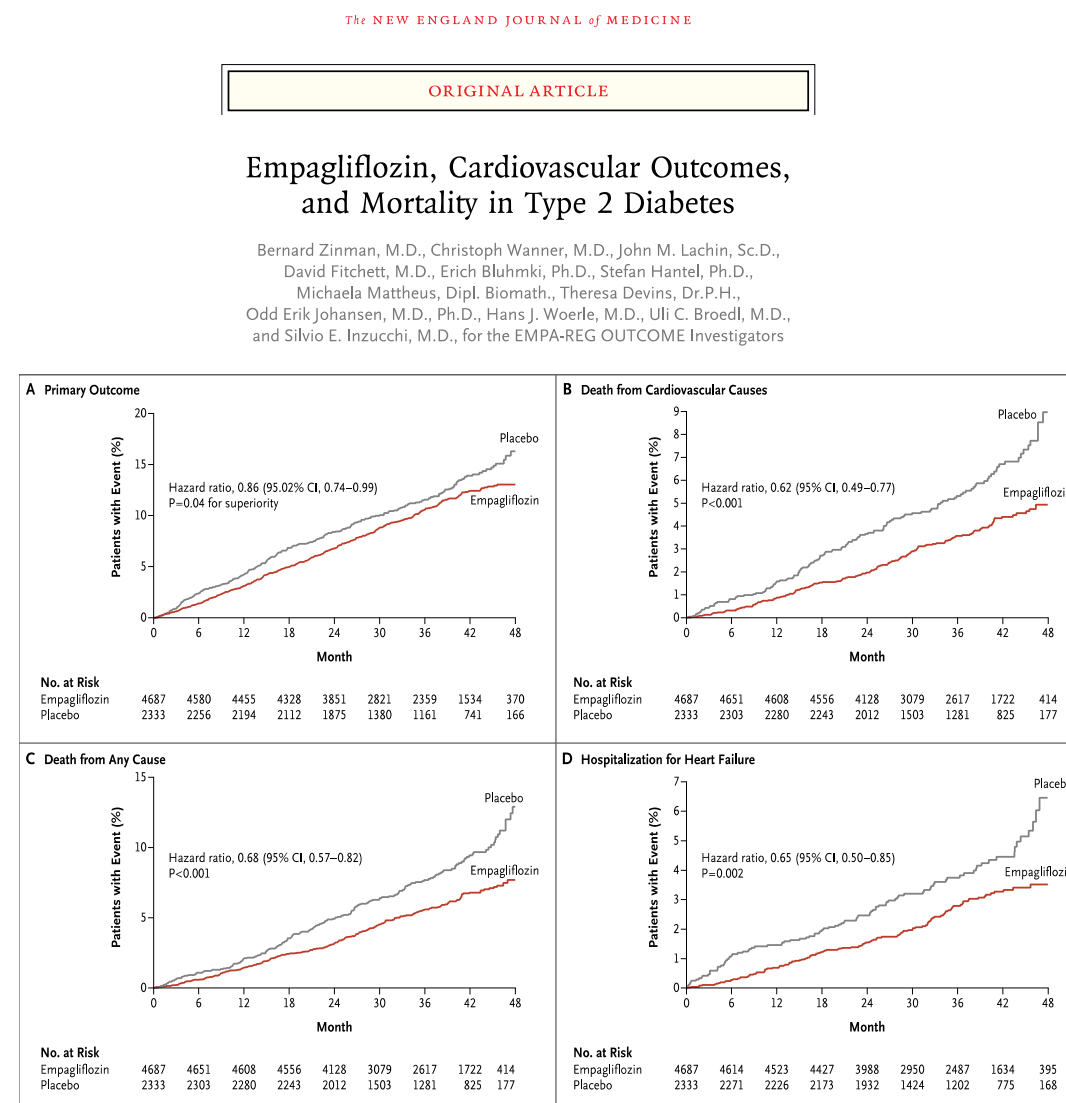


BMJ Open Pioglitazone and cardiovascular outcomes in patients with insulin resistance, pre-diabetes and type 2 diabetes: a systematic review and meta-analysis

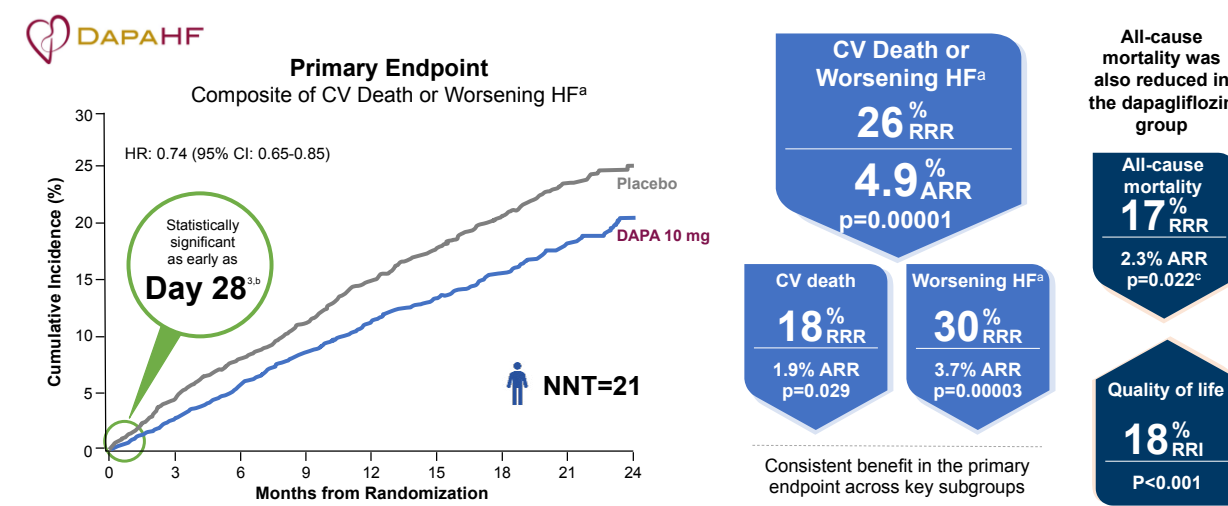
COME TUTTO È INIZIATO



Come tutto è iniziato

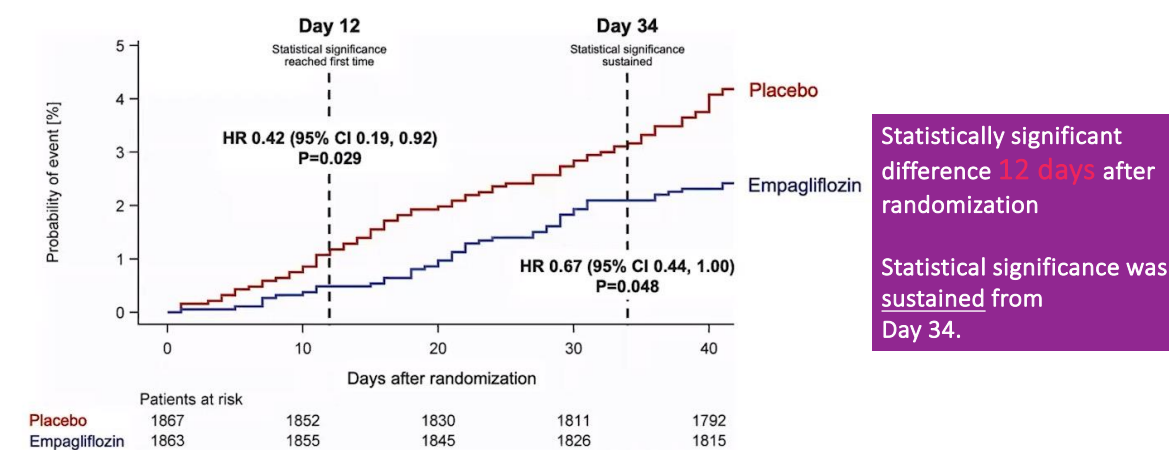


SCOMPENSO CARDIACO A FRAZIONE DI EIEZIONE RIDOTTA



^aHF or an urgent HF visit; ^bPost-hoc analysis; ^cNominal p-value.
 1. McMurray JJV et al. *N Engl J Med*. 2019;381(21):1995-2008; 2. McMurray J. Presented at: ESC Congress; August 31-September 4, 2019; Paris, France; 3. Berg DD et al. *JAMA Cardiol*. 2021;6(5):499-507.

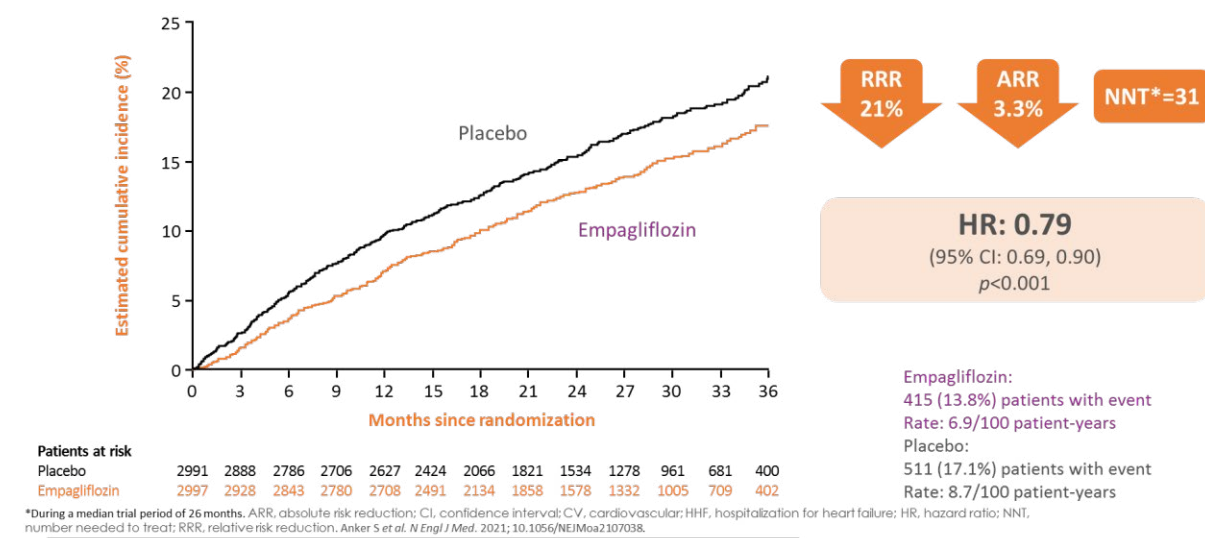
Emperor reduced



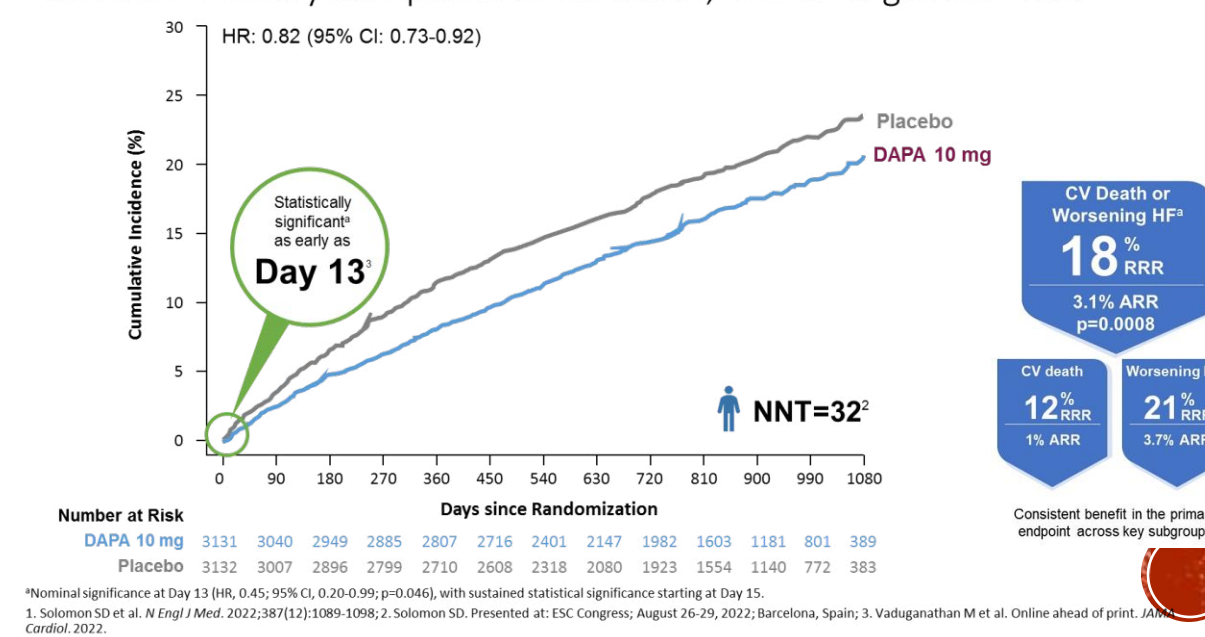
Major outcomes: Time to all-cause mortality, hospitalization for heart failure, or emergency department or urgent care visits for heart failure requiring IV therapy

**SCOMPENSO CARDIACO
 A FRAZIONE DI
 IEZIONE LIEVEMENTE
 RIDOTTA O PRESERVATA**

Emperor-preserved: Empagliflozin demonstrated a clinically meaningful 21% RRR in the composite primary endpoint of CV death or HHF



DELIVER- Primary Composite of CV Death, hHF or Urgent HF Visit¹

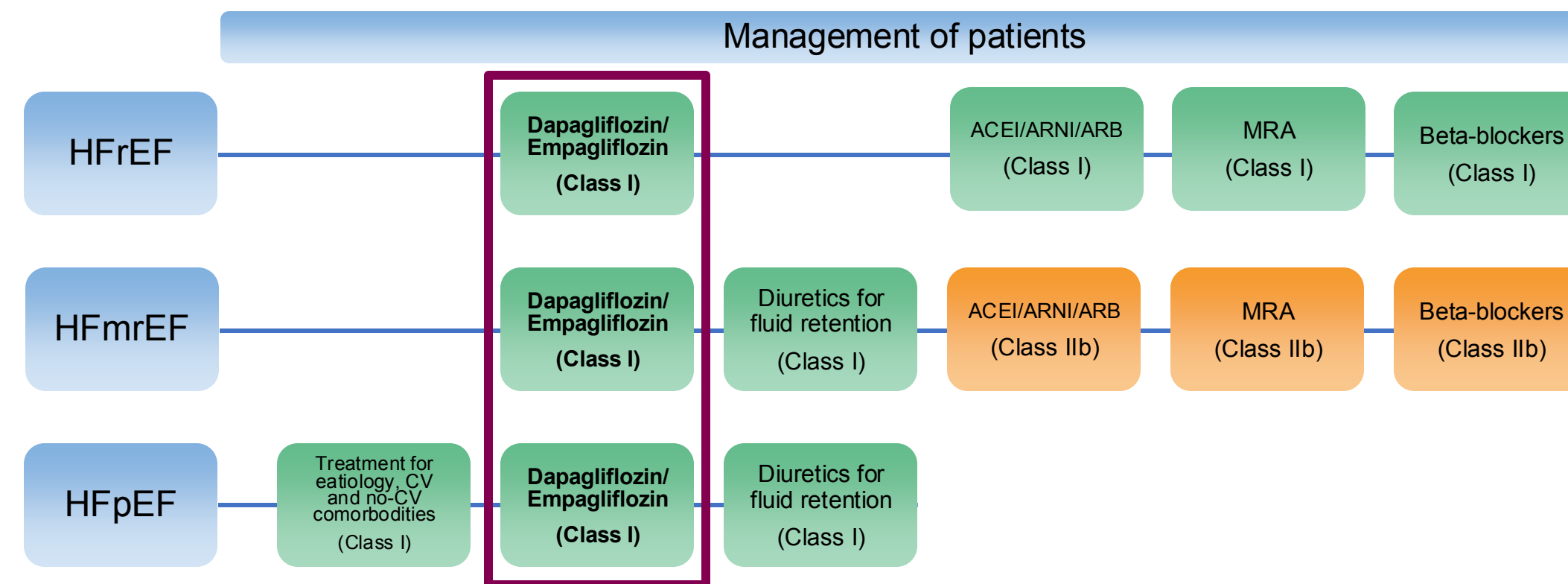




One for all



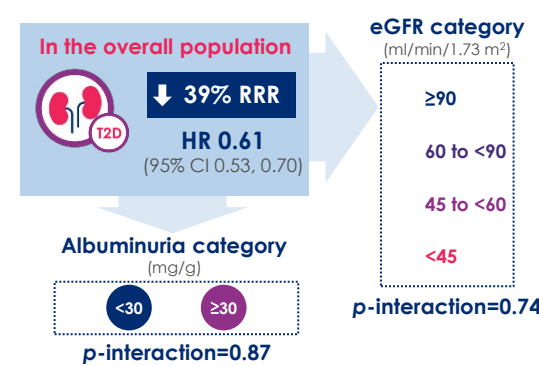
ESC Heart Failure Guidelines: Class IA Recommendation for SGLT2-i in Patients With HF



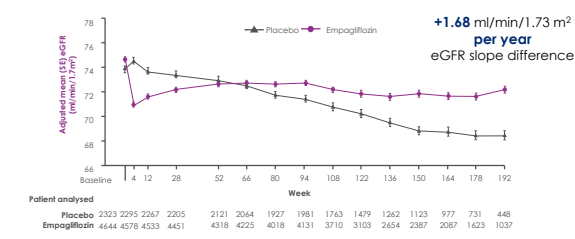
Adapted from: McDonagh TA et al. Eur Heart J. 2021; McDonagh TA et al. Online ahead of print. Eur Heart J. 2023.

EMPA-REG OUTCOME: improvement in kidney outcomes was consistent across kidney-related subgroups

Reduction in the risk of incident or worsening nephropathy^{†1}



Rate of kidney function decline was reduced with empagliflozin compared with placebo²



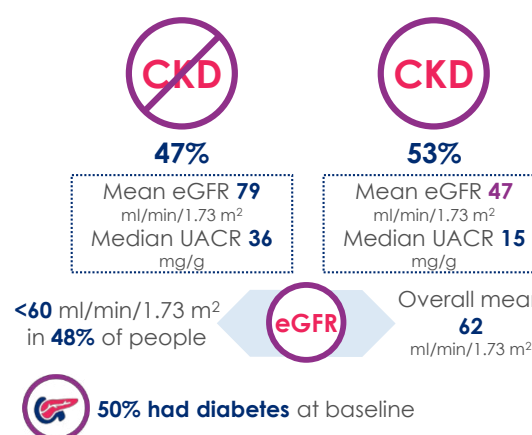
The safety profile of empagliflozin was consistent across baseline eGFR subgroups (≥60 and <60 ml/min/1.73 m²)¹

Events consistent with acute kidney failure, including AKI and hyperkalemia were reported in a lower percentage of people in the empagliflozin group than in the placebo group¹

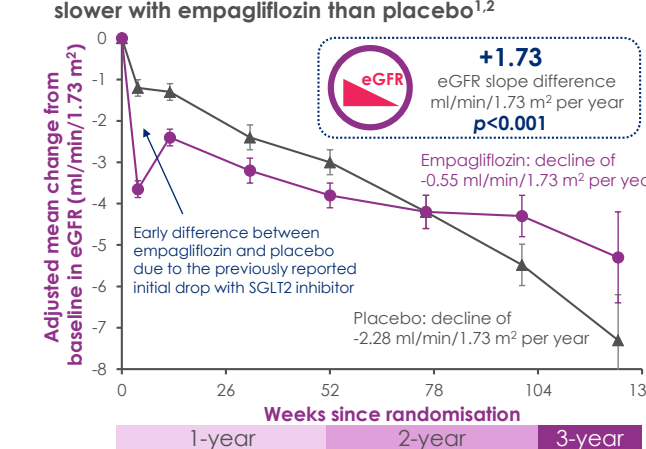


EMPEROR-Reduced: empagliflozin slowed the rate of kidney function decline in HFREF, in a population which included people with CKD

Of 3730 people with HFREF^{1,2}:



Rate of long-term kidney function decline was slower with empagliflozin than placebo^{1,2}



EMPEROR-Preserved: empagliflozin slowed the rate of decline in kidney function in people with HFpEF with or without T2D

Of 5988 people with HFpEF¹:

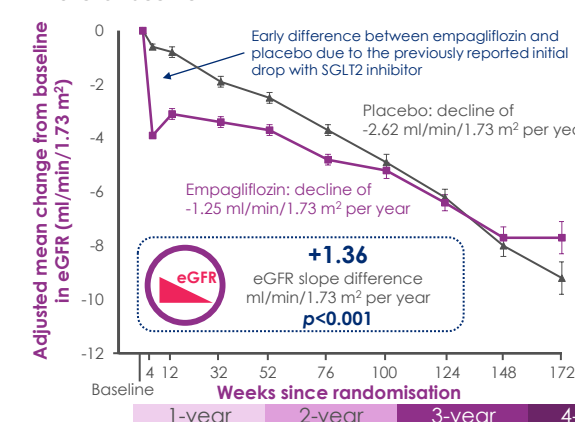


Incidence of the composite kidney outcome in people treated with empagliflozin was similar to placebo¹



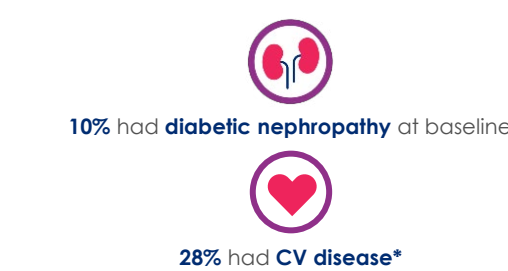
Incidence of acute kidney failure was similar between treatment arms

Empagliflozin reduced the rate of kidney function decline¹

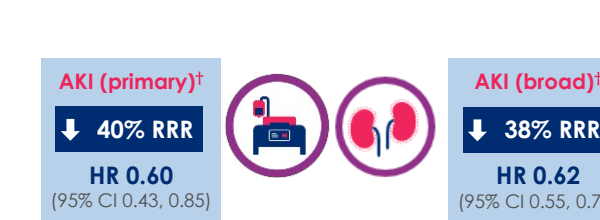


EMPRISE: empagliflozin improved kidney-related safety compared with DPP-4i treatment in the US real-world setting

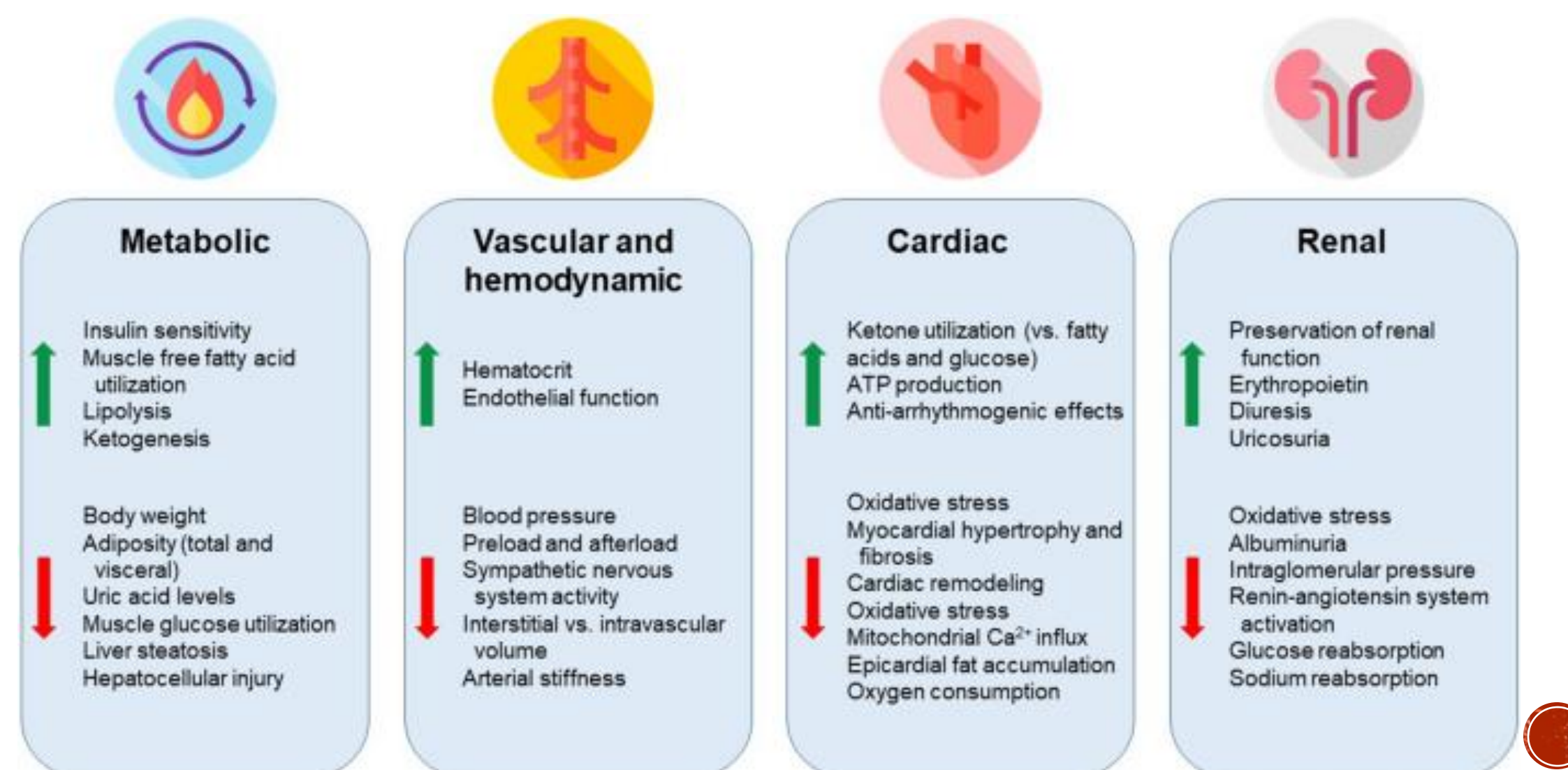
Of 78,144 people with T2D were included in the 3 Year analysis¹:



Empagliflozin reduced the risk of AKI compared with DPP-4i treatment¹



PROTEZIONE CARDIO-NEFRO-METABOLICA

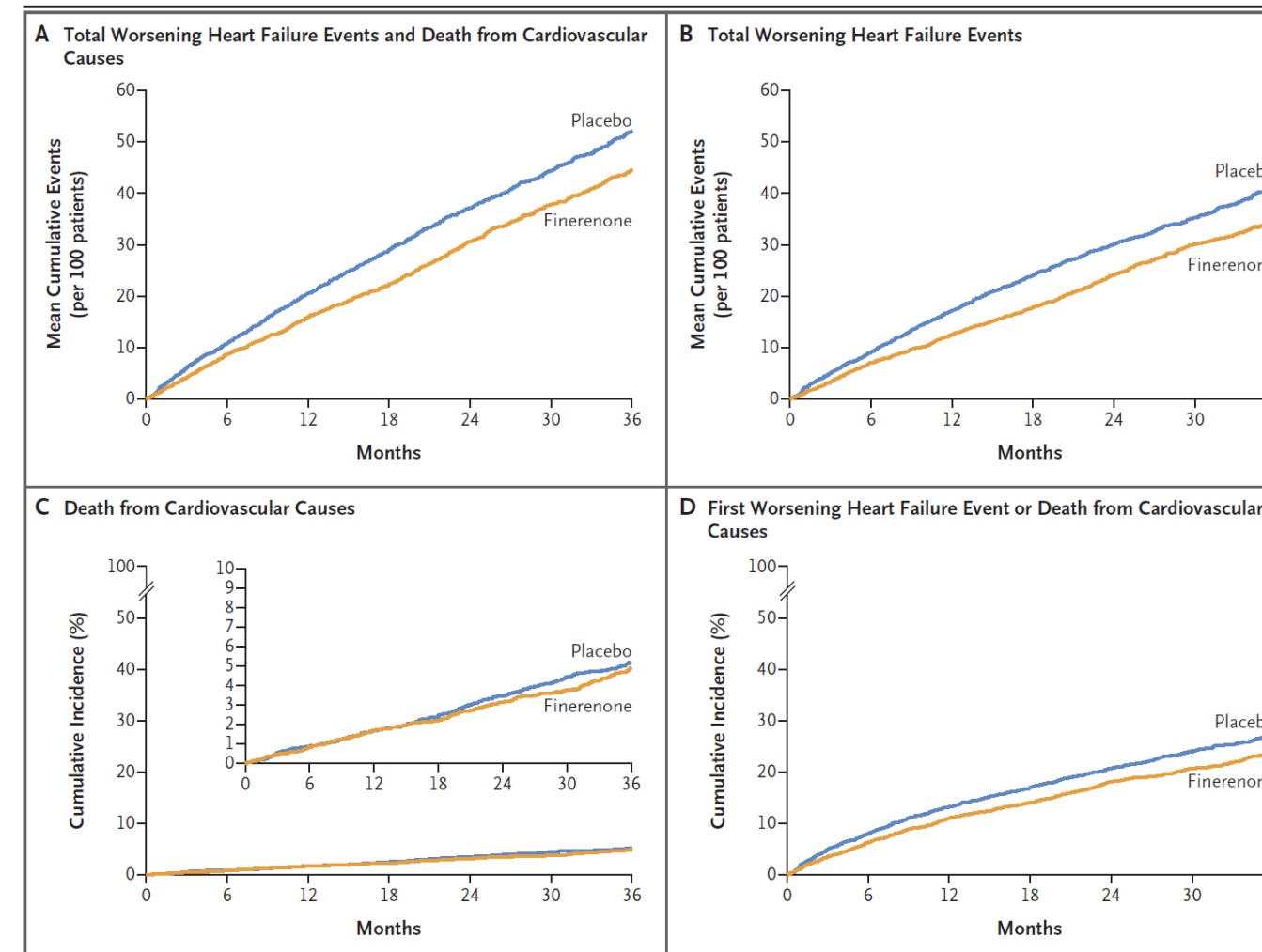


The **NEW ENGLAND**
JOURNAL of *Medicine*

ESTABLISHED IN 1812 OCTOBER 24, 2024 VOL. 391 NO. 16

Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

S.D. Solomon, J.J.V. McMurray, M. Vaduganathan, B. Claggett, P.S. Jhund, A.S. Desai, A.D. Henderson, C.S.P. Lam, B. Pitt, M. Senni, S.J. Shah, A.A. Voors, F. Zannad, I.Z. Abidin, M.A. Alcocer-Gamba, J.J. Atherton, J. Bauersachs, M. Chang-Sheng, C.-E. Chiang, O. Chioncel, V. Chopra, J. Comin-Colet, G. Filippatos, C. Fonseca, G. Gajos, S. Golland, E. Goncalvesova, S. Kang, T. Katova, M.N. Kosiborod, G. Latkovskis, A.P.-W. Lee, G.C.M. Linssen, G. Llamas-Esperson, V. Mareev, F.A. Martinez, V. Melenovskij, B. Merkeley, S. Nodari, M.C. Petrie, C.I. Saldarriaga, J.F.K. Saraiva, N. Sato, M. Schou, K. Sharma, R. Troughton, J.A. Udell, H. Ukkonen, O. Vardeny, S. Verma, D. von Lewinski, L. Voronkov, M.B. Yilmaz, S. Zieroth, J. Lay-Flurrie, I. van Gameren, F. Amarante, P. Kolkhof, and P. Viswanathan, for the FINEARTS-HF Committees and Investigators*



CONCLUSIONS

In patients with heart failure and mildly reduced or preserved ejection fraction, finerenone resulted in a significantly lower rate of a composite of total worsening heart failure events and death from cardiovascular causes than placebo



SEMAGLUTIDE (glp-1 ra) MECCANISMI DI CARDIO-NEFROPROTEZIONE

Effetti Metabolici:

- 1) Riduce la glicemia in modo glucosio-dipendente, stimolando la secrezione di insulina e riducendo la secrezione di glucagone quando la glicemia è elevata
- 2) Riduce l'appetito per azione sul nucleo arcuato a livello ipotalamico che comporta un ridotto apporto calorico e di conseguenza una riduzione del peso corporeo e della massa grassa
- 3) Miglioramento dei lipidi plasmatici e una riduzione della pressione arteriosa sistolica e diastolica (azione anti-aterosclerotica)

Effetti Nefroprotettivi:

- 1) Attenuazione della velocità di declino del filtrato glomerulare stimato (eGFR) e riduzione dell'albuminuria nel tempo

Effetti Anti infiammatori:

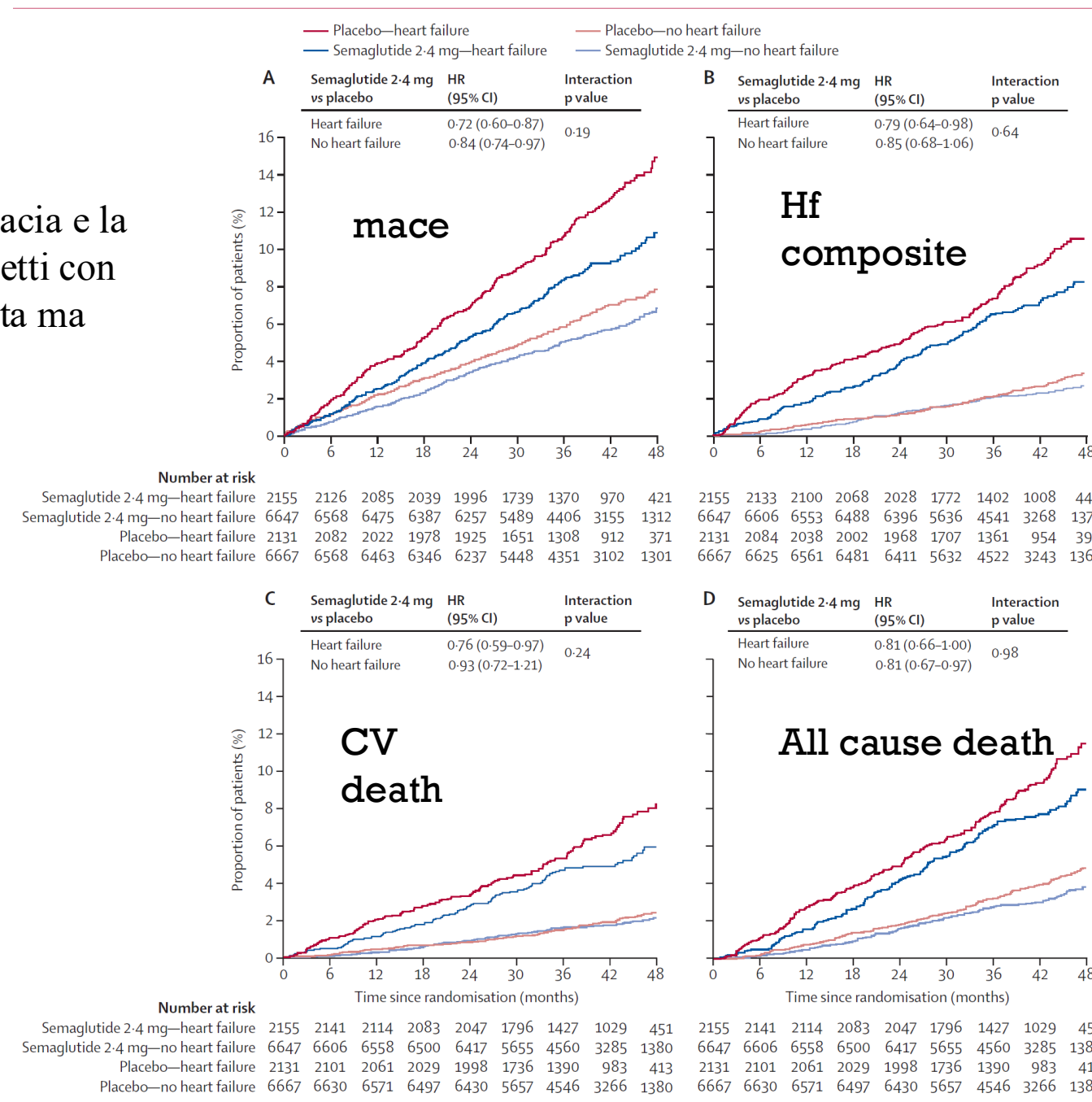
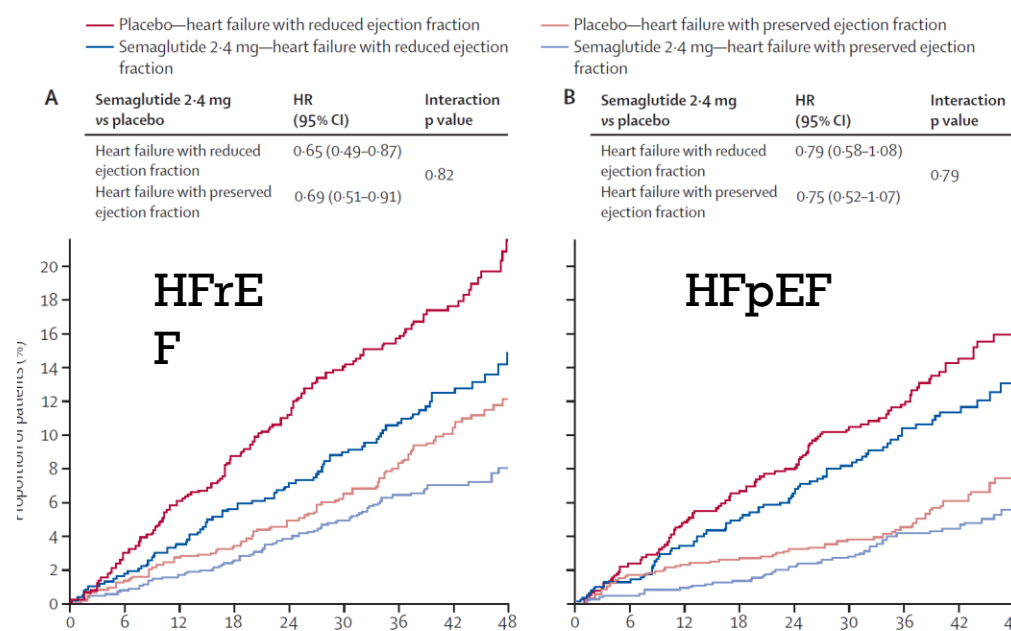
- 1) riduzione dei livelli di citochine pro-infiammatorie
- 2) modulazione dell'attività del sistema immunitario



Semaglutide and cardiovascular outcomes in patients with obesity and prevalent heart failure: a prespecified analysis of the SELECT trial

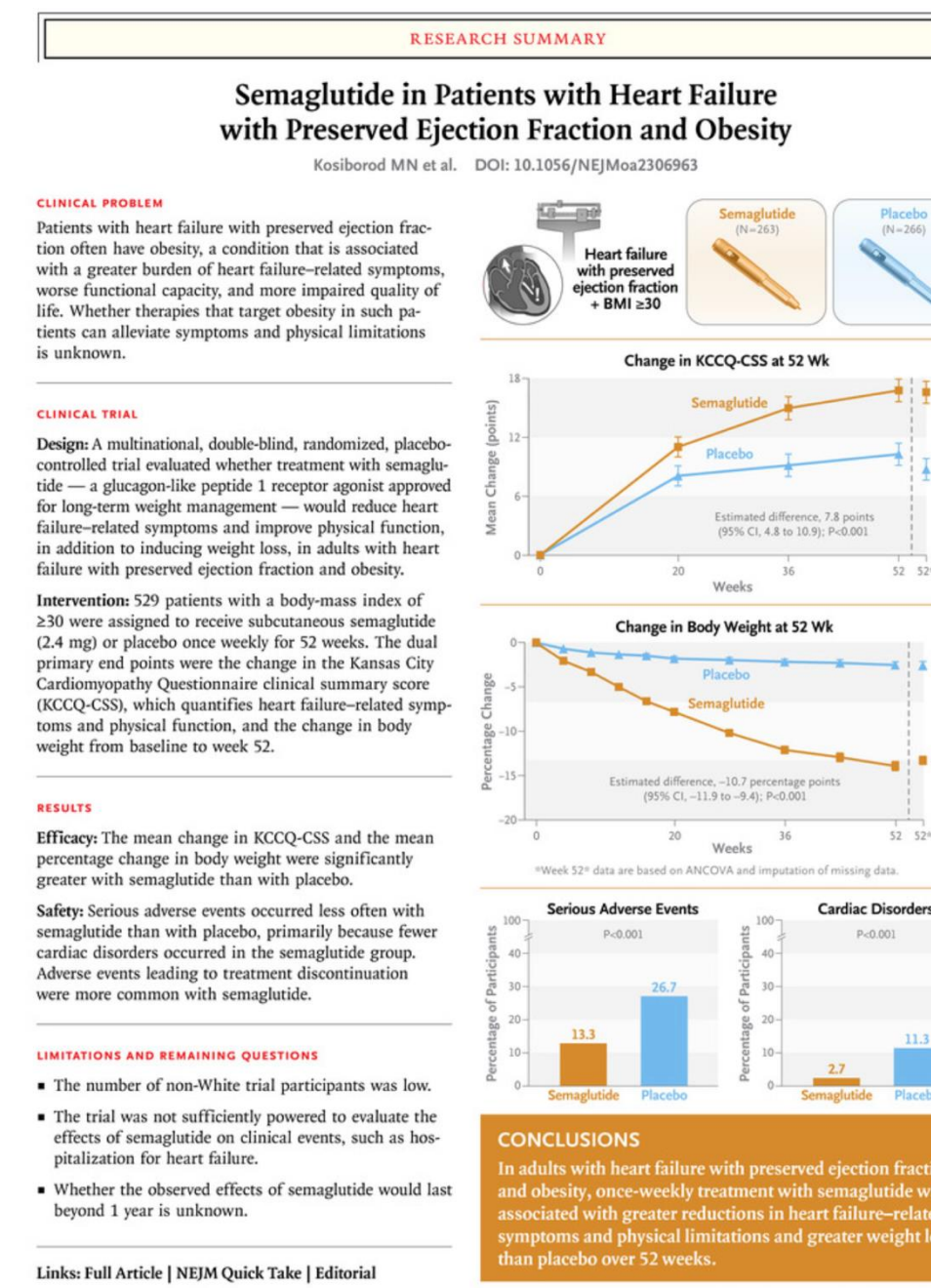
John Deanfield, Subodh Verma, Benjamin M Scirica, Steven E Kahn, Scott S Emerson, Donna Ryan, Bidiko Lingway, Helen M Colhoun, Jorge Plutzky, Mikhail N Kosiborod, G Kees Hovingh, Soren Hardt-Lindberg, Ofir Frenkel, Peter E Weeke, Soren Rasmussen, Assen Goudeev, Chim C Lang, Miguel Uribe-Triano, Mikko Pietila, A Michael Lincoff, for the SELECT Trial Investigators

Lo studio SELECT ha recentemente valutato l'efficacia e la sicurezza di semaglutide 2,4 mg s.c. in 17.604 soggetti con $IMC \geq 27$ kg/m² e una storia di ASCVD documentata ma senza diabete tipo 2 noto



SEMAGLUTIDE STEP-HF_pEF TRIAL

- 529 pazienti con scompenso cardiaco con funzione cardiaca preservata e obesità (BMI >30)
- Semaglutide (2.4 mg a settimana) vs placebo per 52 settimane.
- End point primari: Variazione del Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS; valori da 0 a 100, valori più alti indicano meno sintomi e meno limitazione fisica) e cambiamento del peso corporeo .
- End point secondari: 6MWT, composito di morte, scompenso cardiaco, cambiamenti nel KCCQ-CSS e 6MWT, cambiamenti nei valori di PCR.
- **Risultati:** variazione KCCQ-CSS 16.6 points in semaglutide , 8.7 in placebo (differenza stimata 7.8 punti; 95% [CI], 4.8 a 10.9; P<0.001), cambiamento peso corporeo -13.3% in semaglutide e -2.6% in placebo (differenza -10.7 punti percentuali; 95% CI, -11.9 a -9.4; P<0.001).
- Eventi avversi seri : 35 partecipanti (13.3%) in semaglutide , 71 (26.7%) in placebo.
- **Conclusioni:** Nei pazienti con scompenso cardiaco a funzione sistolica preservata e obesità il trattamento con semaglutide (2.4 mg) porta a riduzione dei sintomi e incremento della capacità di esercizio e perdita di peso rispetto a placebo.



PROPOSTE DI NUOVI MODELLI GESTIONALI

TARGET SFIDANTI CON FORTI RICADUTE PROGNOSTICHE

VALUTAZIONE CARDIO-METABOLICA «OLISTICA» DEL PZ

FARMACI EFFICACI

VALUTAZIONE MMG
 ↓
CUP
 ↓
CONSULENZA CARDIOLOGICA



EQUIPE DI CURA MULTIDISCIPLINARE

MMG:

- ATTREZZATURE DIAGNOSTICHE

INFERMIERE:

- DEVICE PER TELEMONITORAGGIO
- POINT OF CARE
- AMBULATORI VALUTAZIONE RISCHIO CARDIOVASCOLARE

CARDIOLOGO:

- AMBULATORI IN SEDE CON SLOT DEDICATI AI MMG DELLA CASA DI COMUNITA'
- ATTIVITA' DI «HEART TEAM» TERRITORIALE



DIMISSIONE OSPEDALIERA:

- OTTIMIZZAZIONE DELLE CURE
- PIANIFICAZIONE DI FOLLOW-UP

TELEMONITORAGGIO:

- RILEVAZIONE MULTIPARAMETRICA NEL PRIMO MESE CRITICO POST DIMISSIONE

TELEVISITA:

- IMPLEMENTAZIONE RAPIDA DELLA TERAPIA POST DIMISSIONE E VERIFICA DEI TARGET

AMBULATORIO DEDICATO FOLLOW-UP A 1 MESE

PROGRAMMI DI TELERIABILITAZIONE



CONNECT CHF/CKD
Progetto telemonitoraggio post dimissione scompenso cardiaco
AZIENDA USL TOSCANA CENTRO



Durante la fase di telemonitoraggio, tutti i dati sono accessibili anche al MMG ed al Nefrologo in modo da identificare e risolvere eventuali criticità emerse. In particolare, visto che la funzione renale rappresenta un fattore critico potenzialmente limitante la corretta up-titration della terapia, sono previsti momenti preordinati di confronto con il nefrologo per la discussione dei casi più complessi

Dimissione Ospedaliera dopo SC:

Segnalazione al MMG della dimissione del pz e trasmissione di password per accedere al portale di monitoraggio

Pz ad alto profilo di rischio: consegna di Kit di telemonitoraggio con rilevazione autonoma, giornaliera dei parametri da effettuare nelle prime 3 settimane dalla dimissione → Visita ambulatorio scompenso

Pz a basso profilo di rischio: attivazione dell'infermiere di famiglia (COT) che con kit di monitoraggio mobile effettua un controllo settimanale nelle prime 3 settimane dalla dimissione → Visita ambulatorio scompenso

Contatto in TELEVISITA a 10 gg dalla dimissione per controllo preordinato di: Creatinina (GFR) e albumina/creatinina urinaria Na-K NTproBNP



