Come semplificare la terapia nel paziente "complesso" con ipertensione arteriosa e/o ipercolesterolemia

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Istituti Clinici Scientifici Maugeri, IRCCS
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Gattico-Veruno

Istituti Clinici Scientifici Maugeri

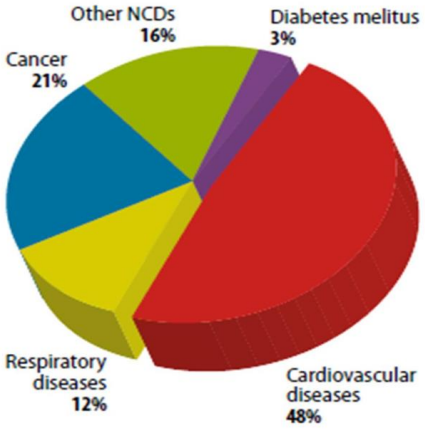
Fonti di finanziamento

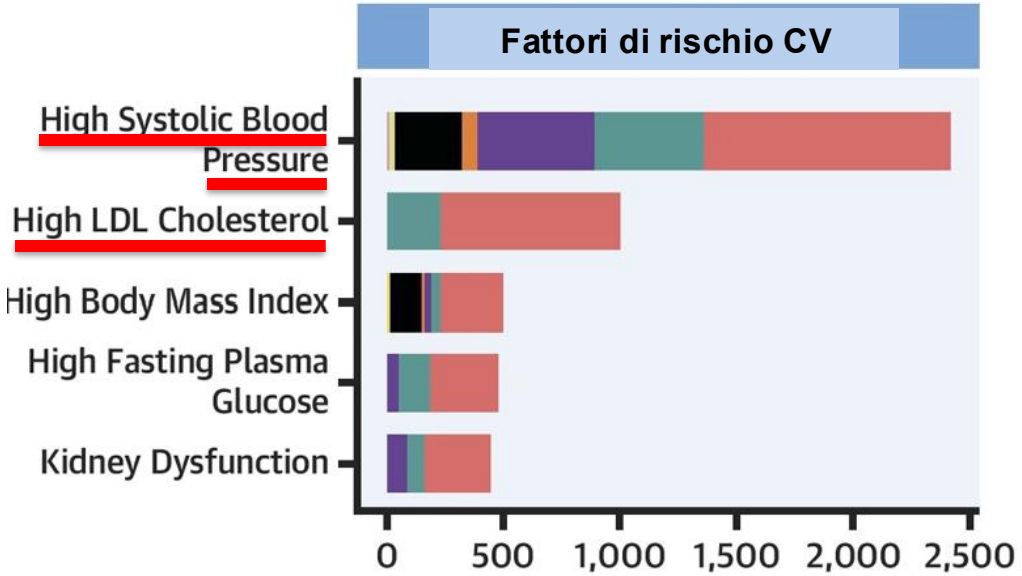
- **Speakers Bureau/Honoraria**: Amarin, Astra Zeneca, Daiichi, Servier, SPA
- **Consulting Fees**: Amarin, Daiichi, Novo Nordisk, SPA
- **Other**: none

Le Malattie Cardiovascolari nel mondo

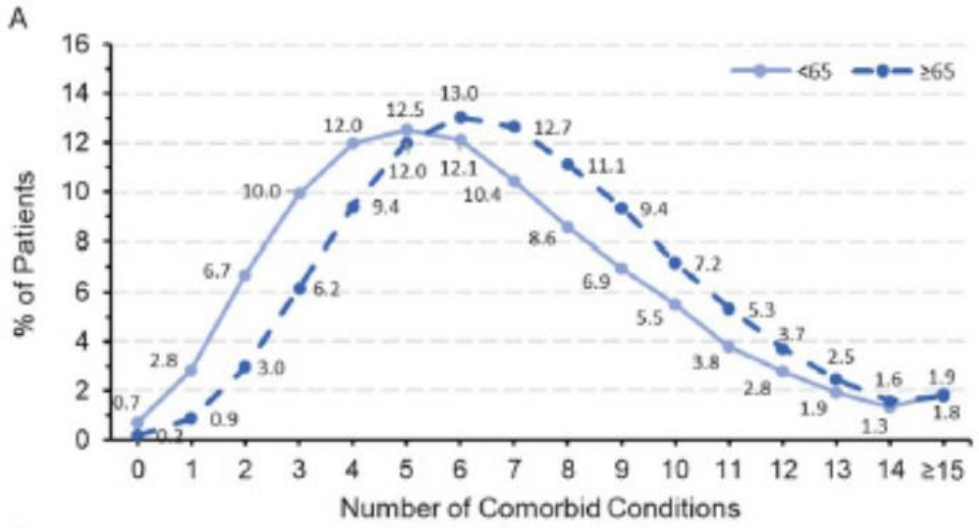
17.3

milioni di morti l'anno





Age-standardized disability-adjusted life years (DALYs) per 100,000



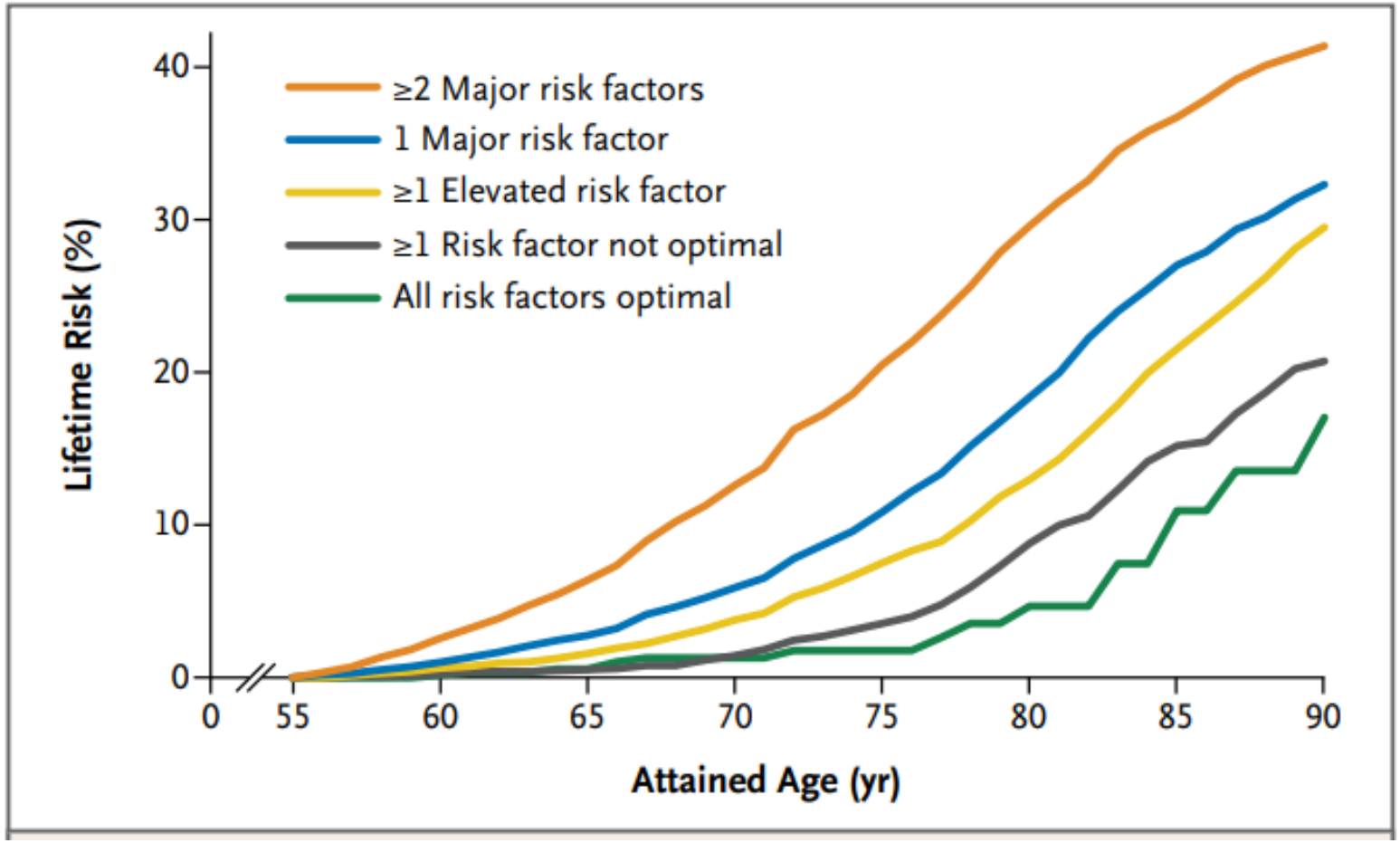
- ✓ Il 98% dei pazienti con ASCVD presentano ≥ 2 comorbidità;
- ✓ la coppia di comorbidità più comune è proprio **ipertensione-dislipidemia** (79%).

Vaduganathan, M. et al. *JACC.* 2022

ORIGINAL ARTICLE

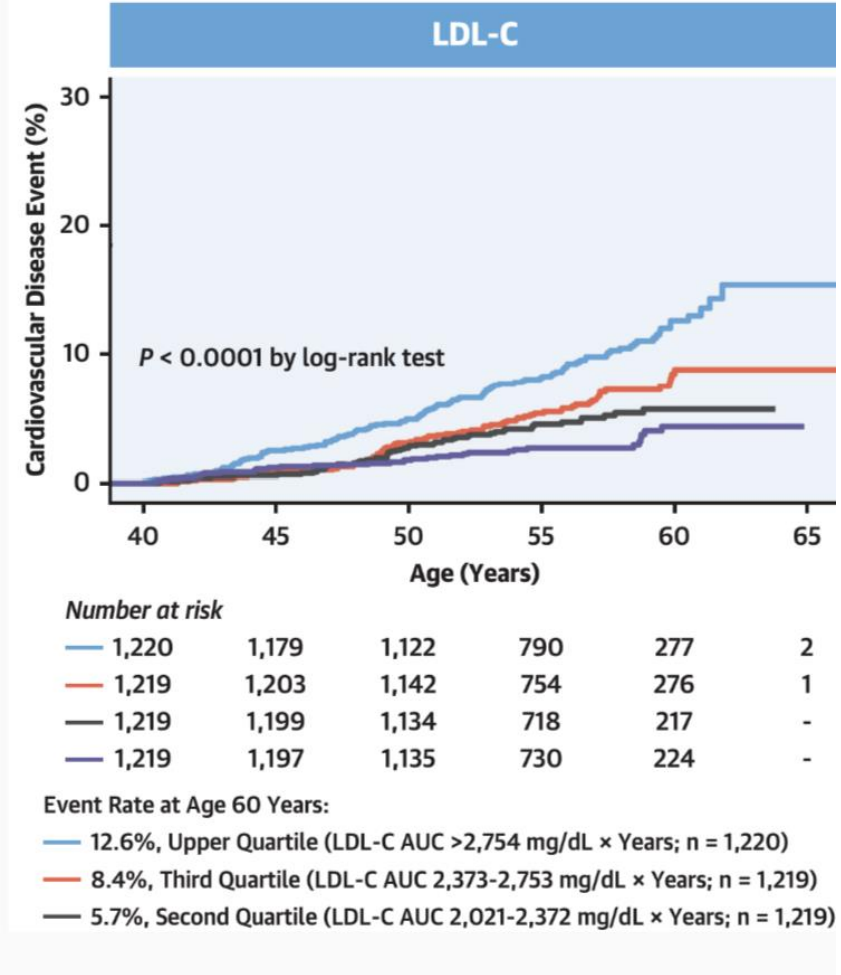
Lifetime Risks of Cardiovascular Disease

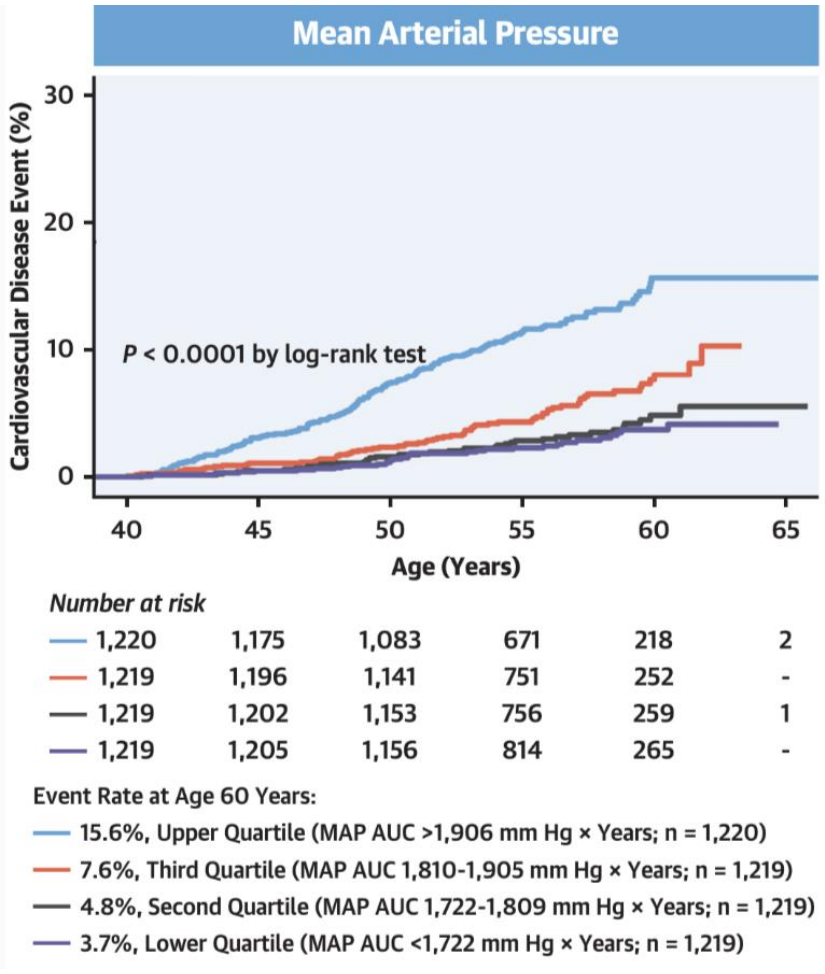
N ENGL J MED 366;4 NEJM.ORG JANUARY 26, 2012



Importanza di ridurre il rischio CV

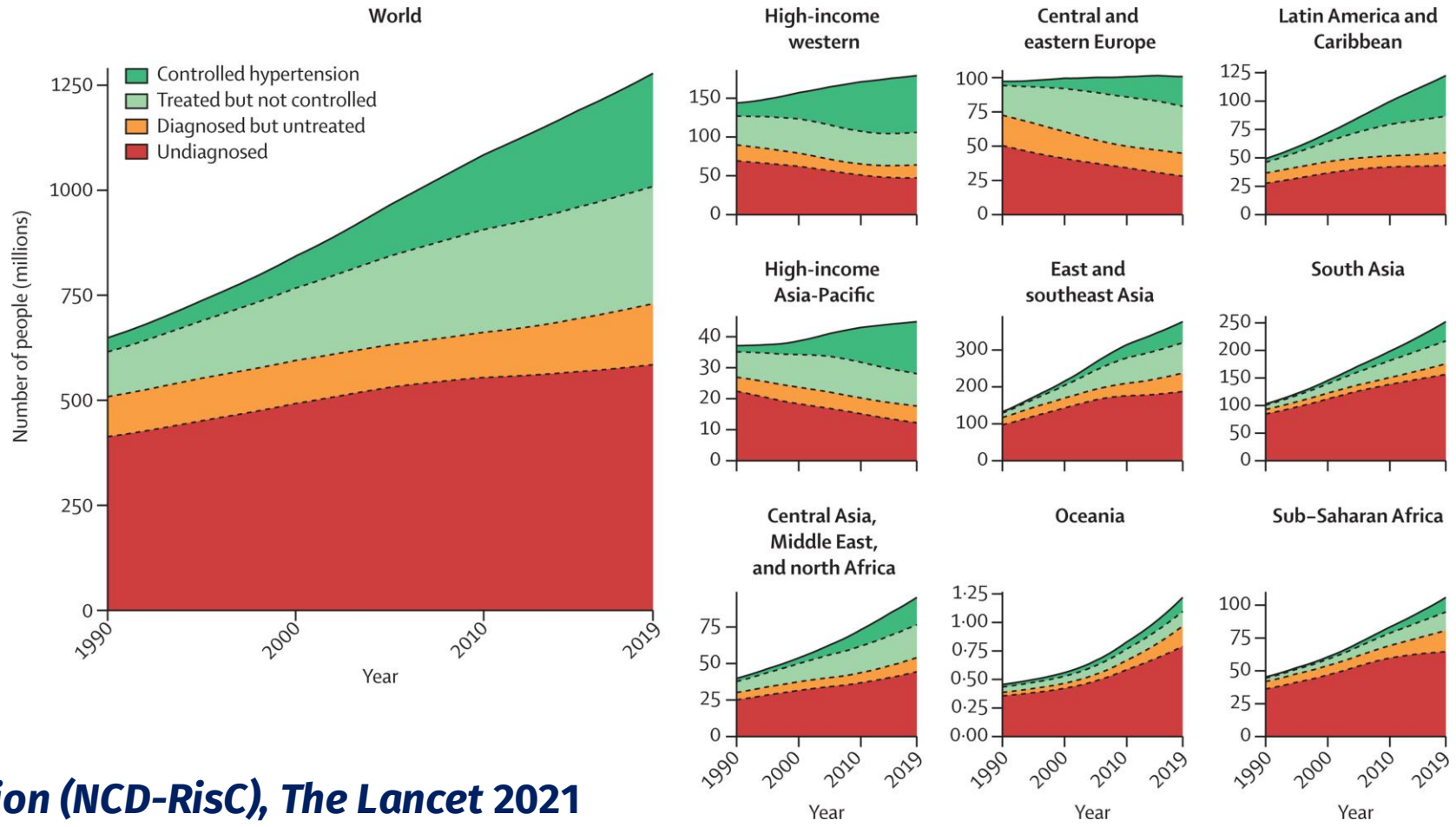
- ✓ Il rischio di Malattie Cardiovascolari aumenta nel tempo ed in modo significativo dal quartile più basso al quartile più alto di esposizione cumulativa (AUC) a **pressione arteriosa e colesterolo LDL**.





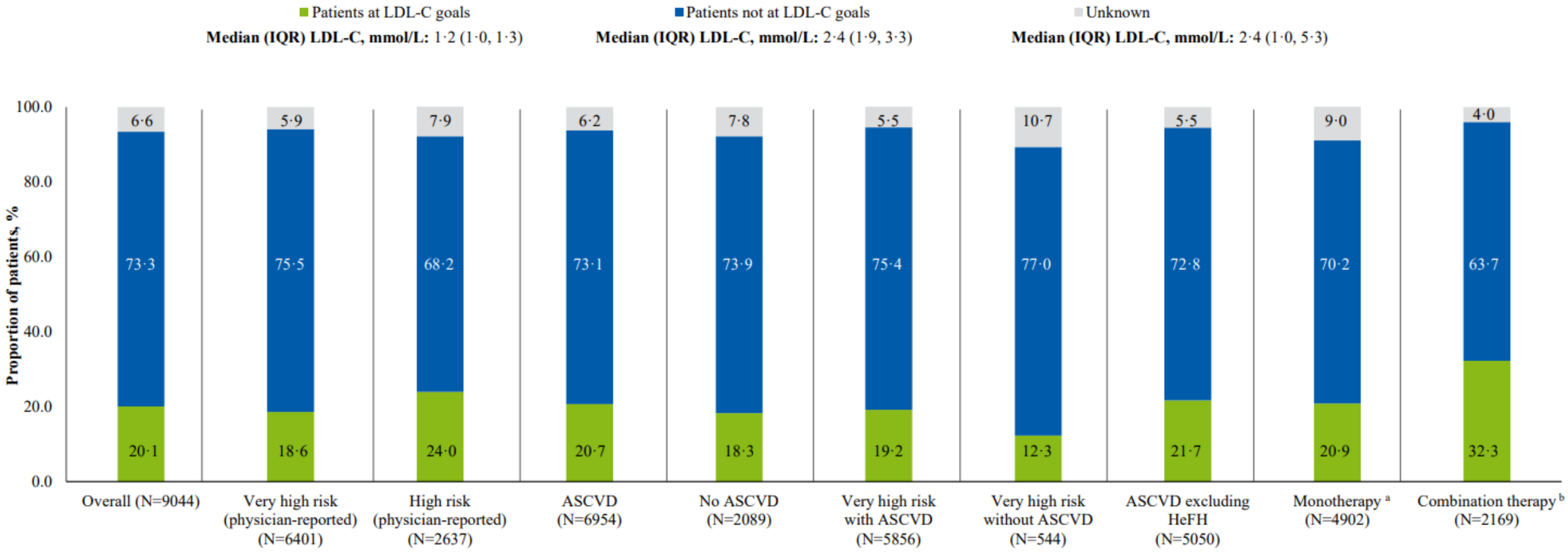
JACC 2023 Mar, 81 (12) 1151–1161

Trends in the number of people with diagnosed, treated and controlled HTN globally and by region, 1990–2019



NCD Risk Factors Collaboration (NCD-RisC), The Lancet 2021

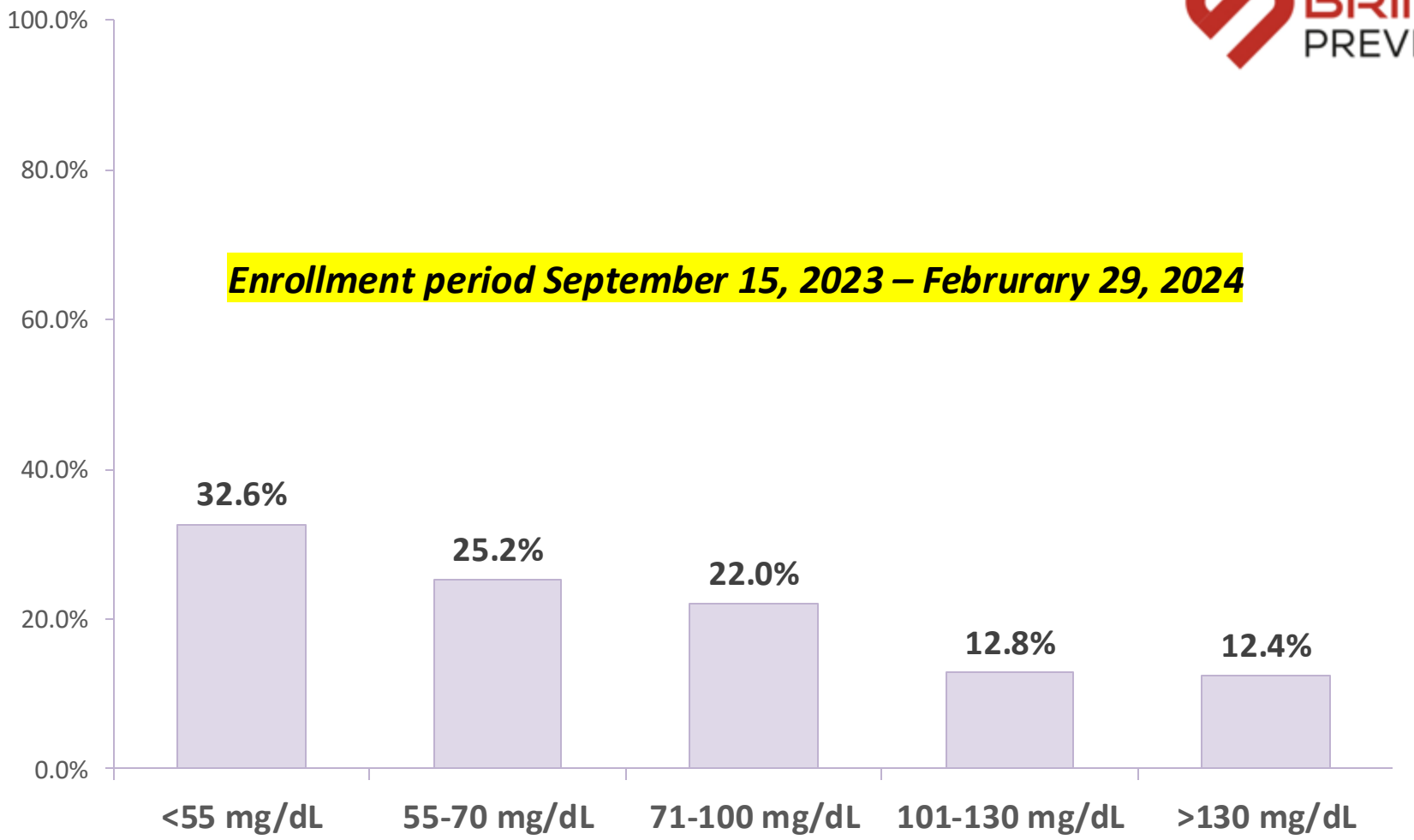
Treatment gaps in the implementation of LDL cholesterol control among high- and very high-risk patients in Europe between 2020 and 2021: the multinational observational SANTORINI study



www.thelancet.com Vol 29 June, 2023

LDL Cholesterol Levels (4783 pts)

BRING•UP PREVENZIONE



Indicazioni al trattamento dell'ipertensione

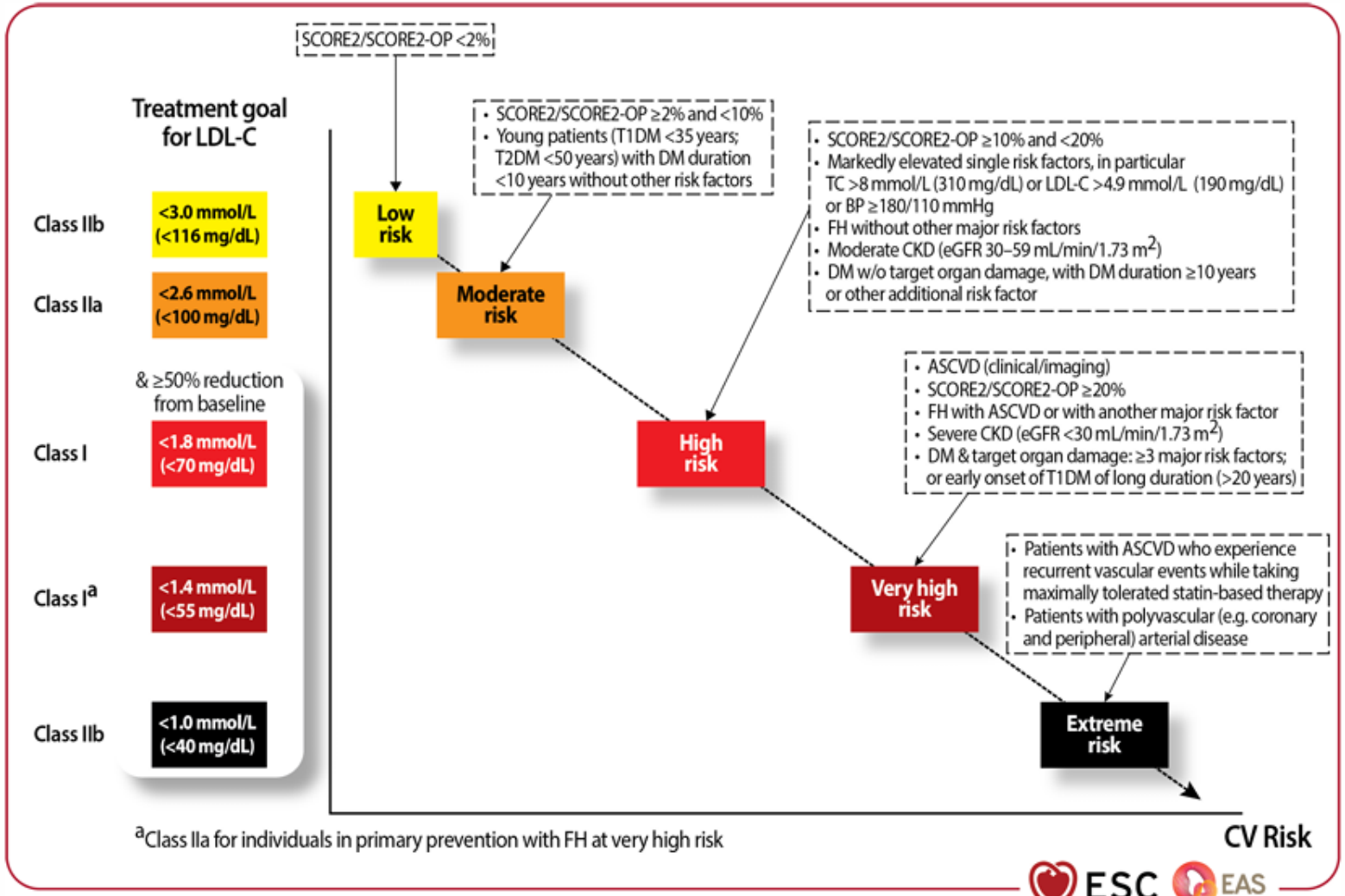
European Society of Hypertension 2023	ESC European Society of Cardiology 2024
Se le misure non farmacologiche falliscono, **il trattamento farmacologico è indicato <u>in tutti i pazienti di età 18-79 anni con PA ≥140/90 mmHg</u>**, indipendentemente dal loro livello di rischio CV (IA). **Se età >80 anni**, il trattamento farmacologico è indicato solo se PA **≥160/90 mmHg** (IB) ma potrebbe essere considerato anche in caso di PA sistolica 140-160 mmHg (IIC)	**Il trattamento farmacologico è indicato <u>in tutti i pazienti con PA ≥140/90 mmHg</u>, contemporaneamente** all'inizio delle misure non farmacologiche, indipendentemente dal loro livello di rischio CV (IA)

Indicazioni alla terapia in caso di PA 130-139/80-89 mmHg

European Society of Hypertension 2023	ESC European Society of Cardiology 2024
Storia di malattia cardiovascolare (principalmente cardiopatia ischemica cronica)	**Storia di malattia cardiovascolare** ma anche... 1. **Diabete mellito** 2. **Nefropatia cronica** 3. **Danno d'organo** 4. **Ipercolesterolemia familiare** 5. **Rischio a 10 anni ≥10%** 6. **Rischio a 10 anni 5-<10% in presenza di modificatori del rischio**

Verdecchia P. et al, Linee guida europee sull'ipertensione. 2024.

Treatment goals for low-density lipoprotein cholesterol across categories of total cardiovascular risk.



2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias (European Heart Journal; doi: 10.1093/eurheartj/ehaf190)

Perché non si raggiungono i targets ?

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

DRUG THERAPY

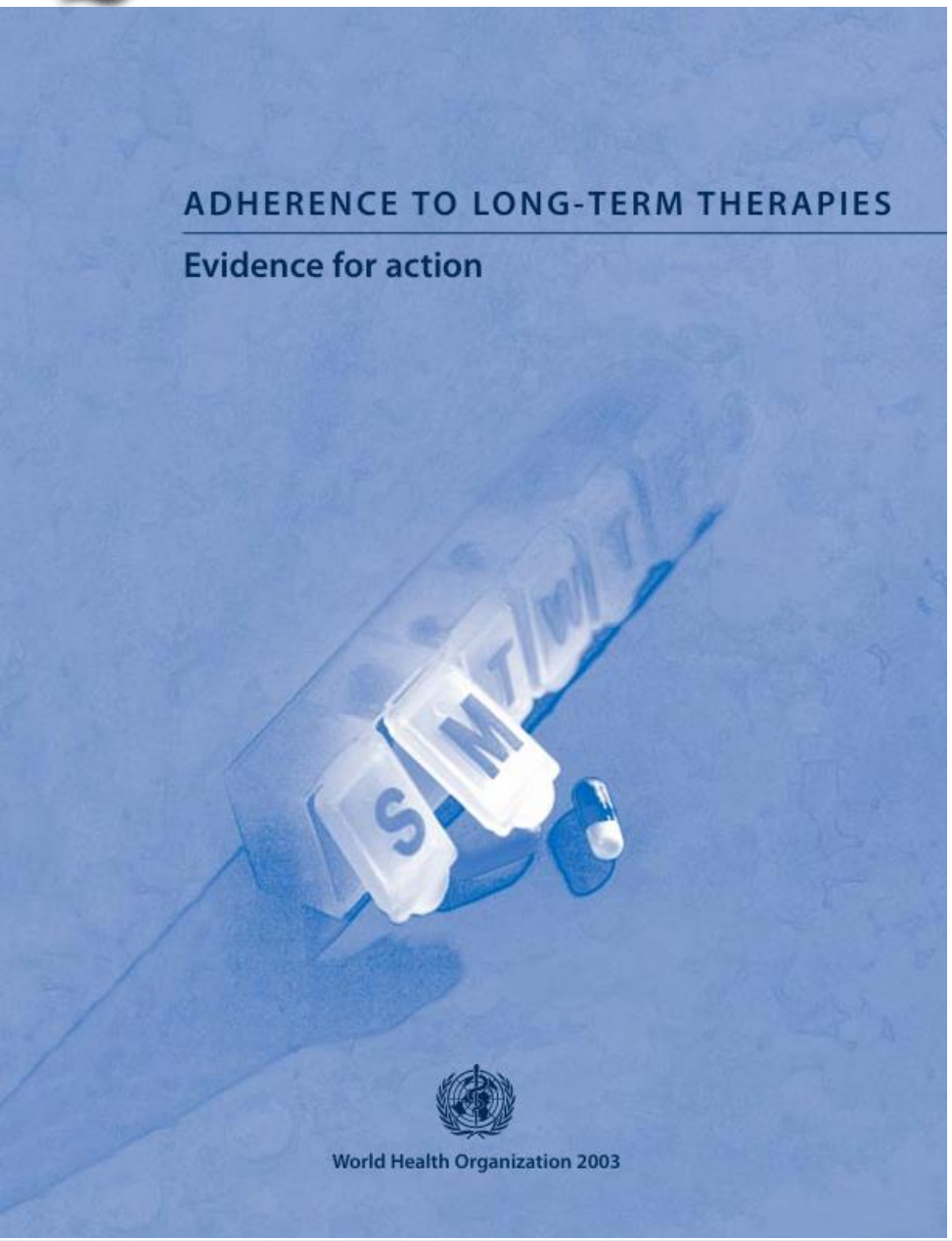
Adherence to Medication

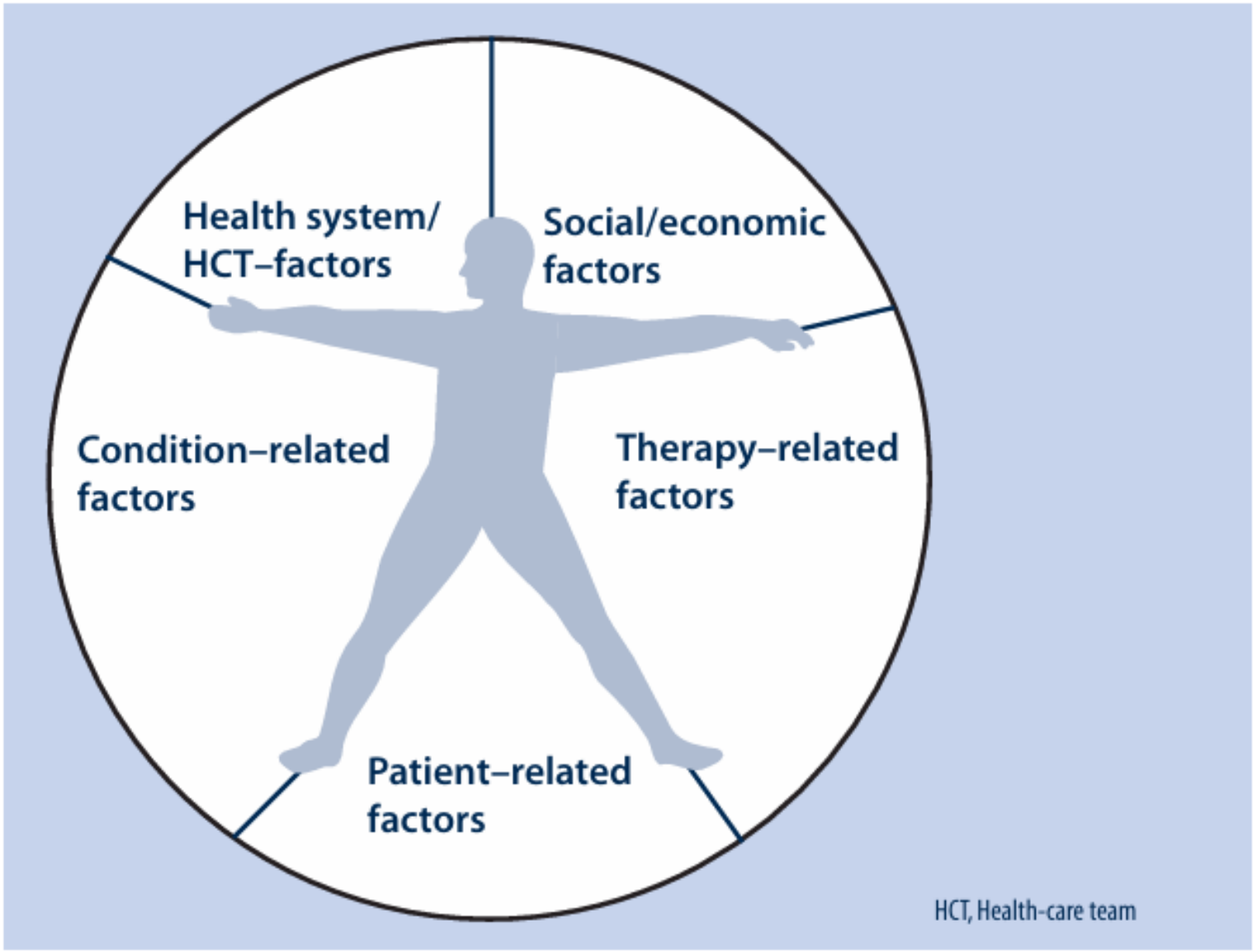
Lars Osterberg, M.D., and Terrence Blaschke, M.D.

Drugs don't work in patients who don't take them.

—C. Everett Koop, M.D.

N Engl J Med 2005;353:487-97

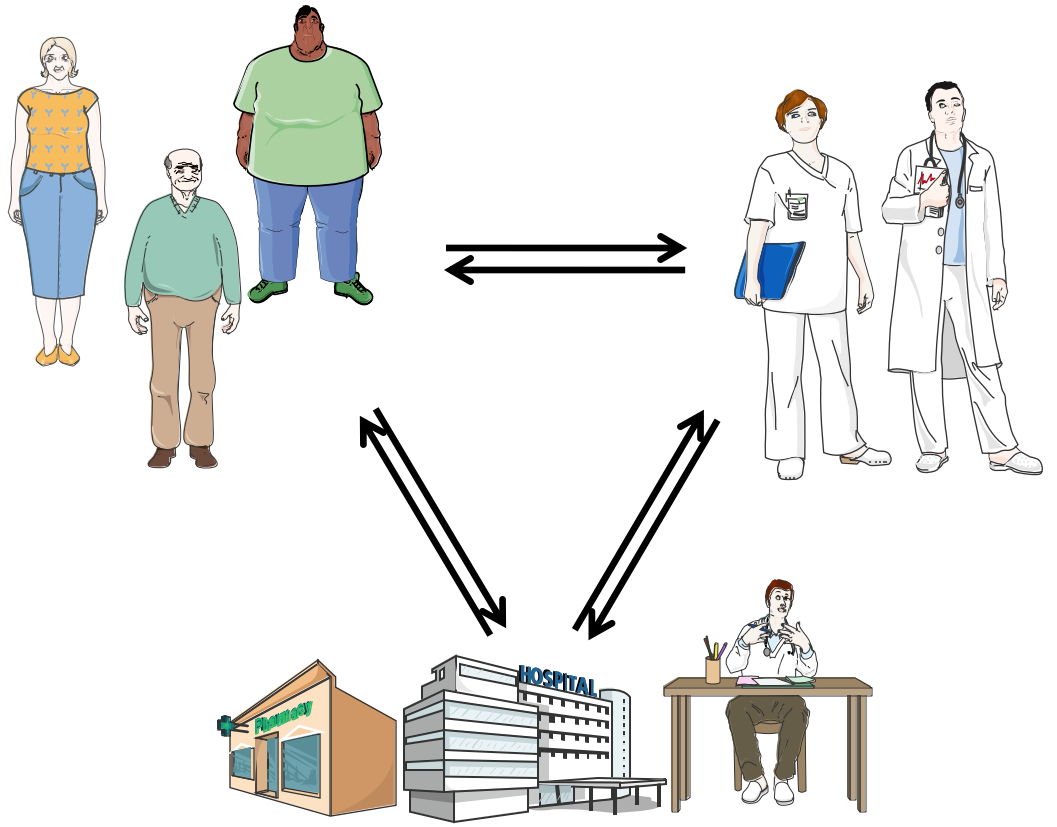

ADHERENCE TO LONG-TERM THERAPIES
Evidence for action
World Health Organization 2003


Health system/
HCT–factors
Social/economic
factors
Condition–related
factors
Therapy–related
factors
Patient–related
factors
HCT, Health-care team

Fattori che influenzano l'aderenza

Paziente

- Età
- Incidenza di comorbilità
- Status sociale
- Remore circa i farmaci ed i loro effetti avversi
- Limitazioni culturali e psicologico/cognitive
- …



Operatore sanitario

- Doti comunicative
- Inerzia terapeutica
- Complessità terapeutica
- *"Prescribing cascade"*
- Scarsa conoscenza del farmaco o del paziente
- …

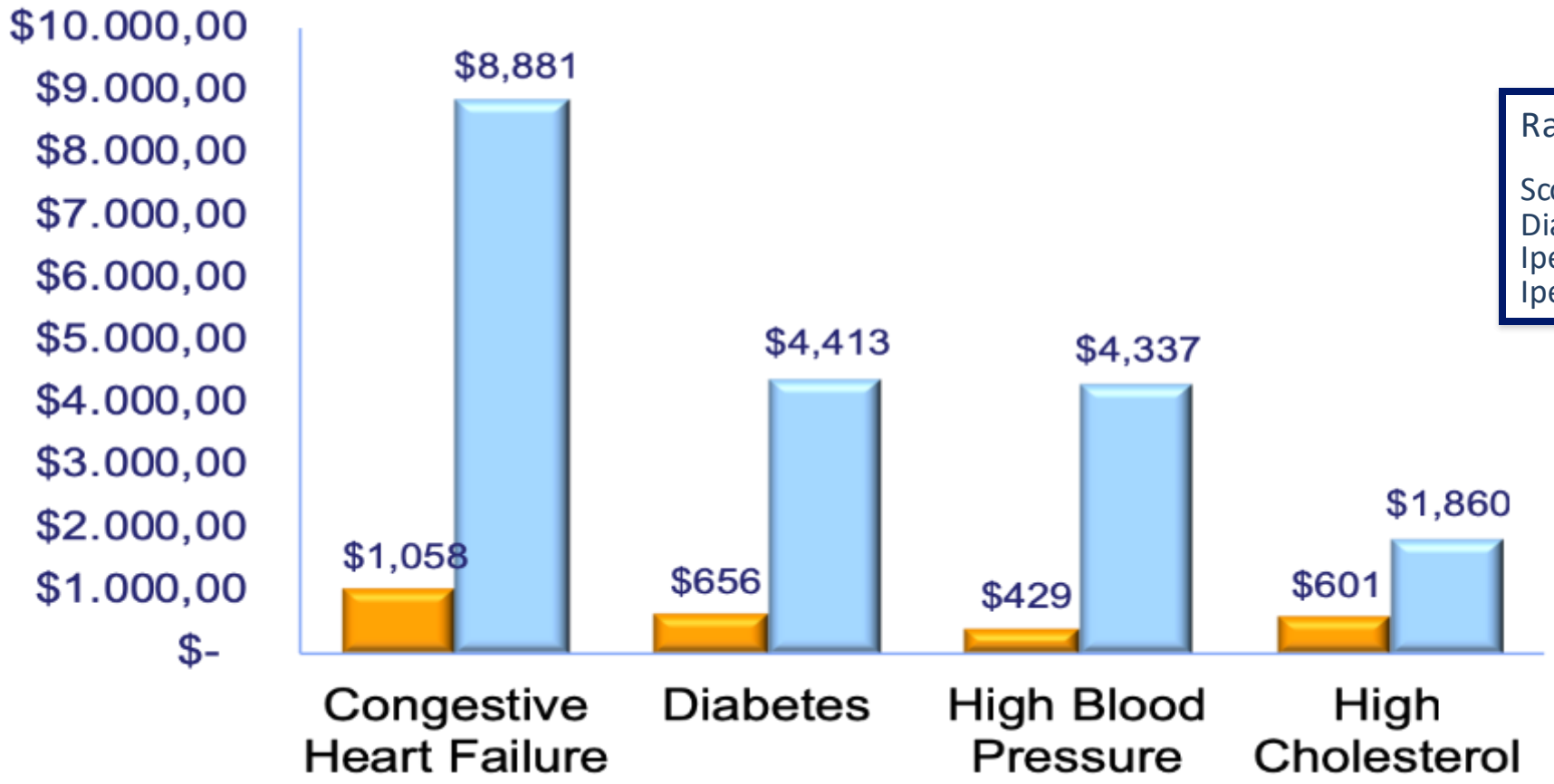
Sistema sanitario

- Sistema di rimborsabilità e/o compartecipazione alla spesa farmaceutica significativa per i pazienti con malattie croniche.
- Accesso alle strutture sanitarie per i follow-up programmati o in caso di emergenza.

Determinanti ambientali e sociali

L'accessibilità al farmaco o alla sua prescrizione, la condizione sociale, l'influenza dei mass media e l'introduzione dei farmaci generici che troppo spesso cambiano di continuo packaging confondendo il paziente.

La non aderenza
Un bilancio economico sfavorevole



Rapporti costo-beneficio :

Scompenso Congestizio : 8.4 : 1
Diabete: 6.7 : 1
Ipertensione arteriosa: 10.1 : 1
Ipercolestrolemia: 3.1 : 1

- **Aumento spesa farmaceutica**
- **Risparmio sulla Spesa sanitaria globale**

Roebuck MC, et al. Health Affairs 2011;30:91-99

TERAPIE E ADERENZA TERAPEUTICA

Ministero della Salute

DIREZIONE GENERALE DELLA PROGRAMMAZIONE SANITARIA

OBIETTIVO

- Promuovere l'appropriatezza nell'uso delle terapie e delle tecnologie diagnostiche e terapeutiche
- Migliorare l'aderenza terapeutica
- Garantire il diritto all'accesso appropriato alle tecnologie diagnostiche e terapeutiche, favorendo l'impiego di strumenti di qualità tecnologica adeguata e di procedure idonee a ottenere risultati sicuri riducendo i potenziali rischi e monitorando nel tempo l'adeguatezza e la qualità

RISULTATI ATTESI

Incremento di soluzioni organizzative che favoriscano l'adesione alle prescrizioni, con particolare riferimento all'aderenza alla terapia farmacologica in caso di trattamenti farmacologici multipli (politerapie)

LINEE DI INTERVENTO PROPOSTE

1. valutare le buone pratiche presenti al fine di individuare un modello nazionale di valutazione dell'appropriatezza prescrittiva, coinvolgendo e responsabilizzando le istituzioni competenti (AIFA, ISS, Agenas ...)
2. promuovere studi di ricerca applicata e soluzioni tecnologiche e organizzative per migliorare l'aderenza terapeutica
3. valutare l'utilizzo delle linee guida e promuoverne l'implementazione per migliorare l'appropriatezza terapeutica e disincentivare l'utilizzo di farmaci non appropriati
4. diffondere le conoscenze sul rischio aumentato di reazioni avverse ai farmaci nei pazienti affetti da patologia cronica e in politerapia
5. sviluppare iniziative per far conoscere i criteri di Beers e di START and STOPP tra gli operatori sanitari
6. favorire l'implementazione di strumenti di ICT di aiuto alla prescrizione con warning per interazioni e controindicazioni
7. adottare procedure che favoriscano l'adesione alle prescrizioni mediche, con particolare riferimento all'aderenza alla terapia farmacologica in caso di trattamenti farmacologici multipli (politerapie)
8. definire modalità organizzative che consentano equità di accesso alle terapie e alle tecnologie, valorizzando le competenze dei centri specializzati a più alto livello di organizzazione
9. formare e informare le persone con cronicità e tutti gli operatori sanitari e non sanitari coinvolti sull'uso appropriato delle terapie e delle tecnologie

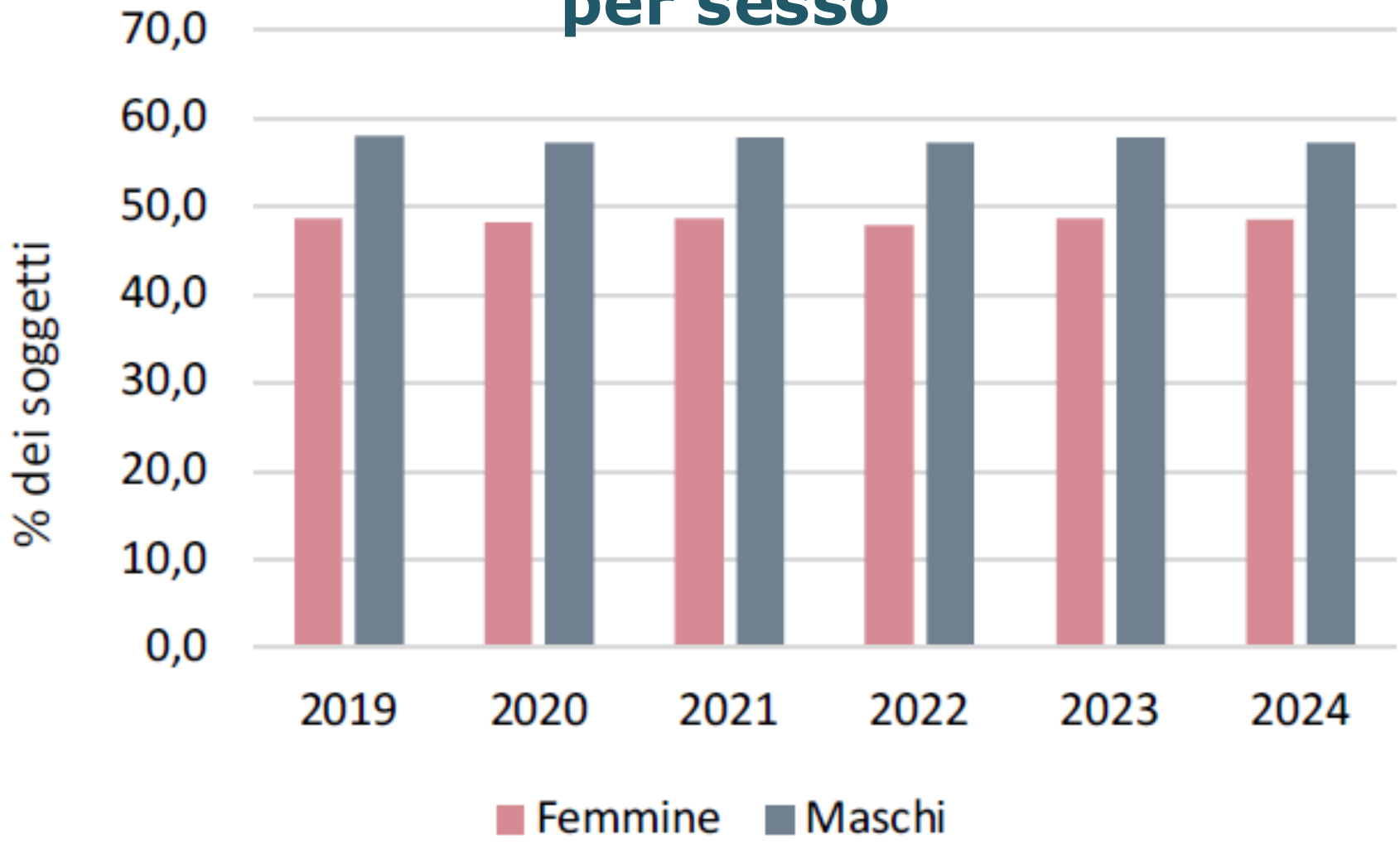
L'uso dei Farmaci in Italia

Rapporto Nazionale

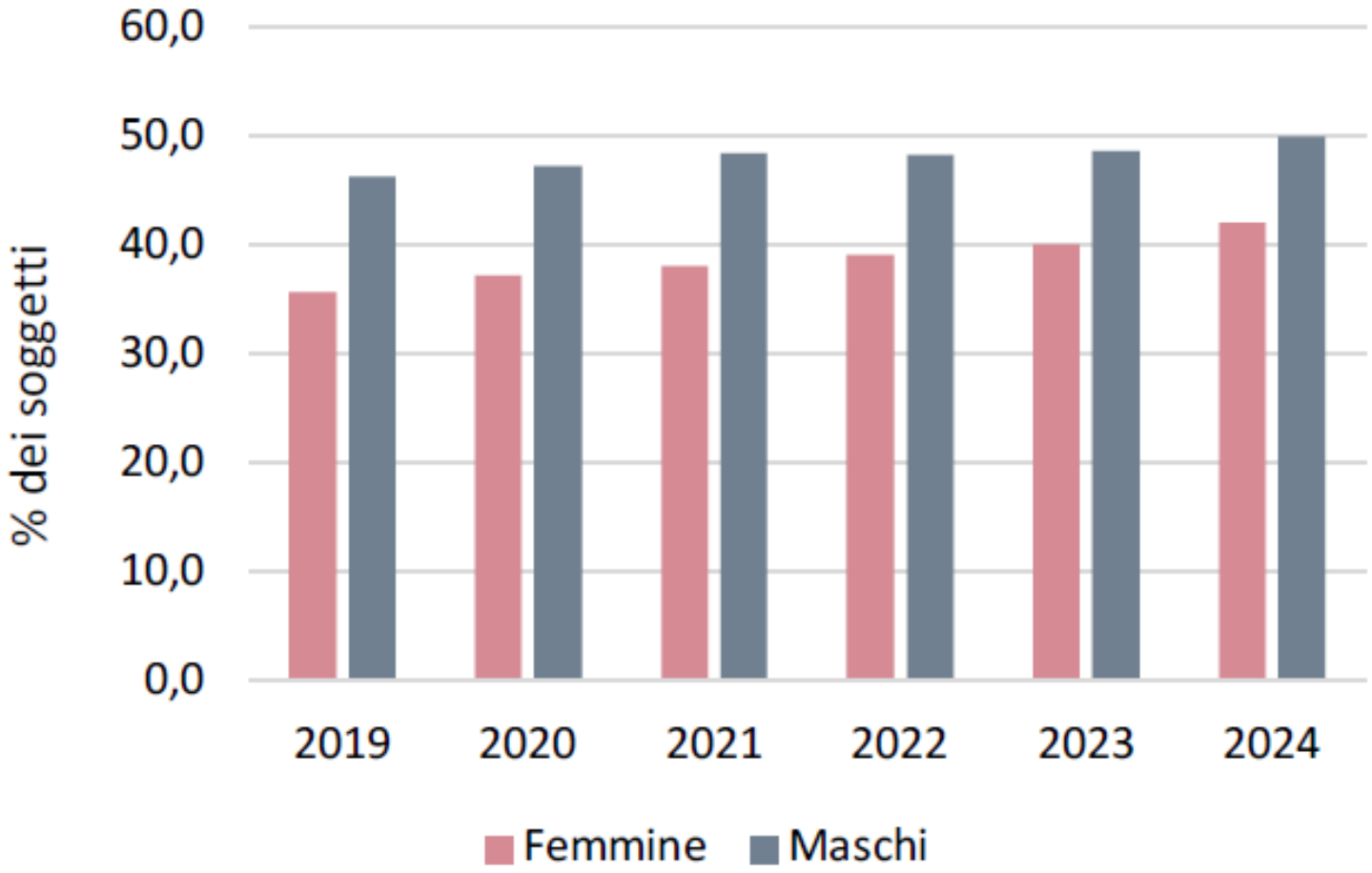
Anno 2024

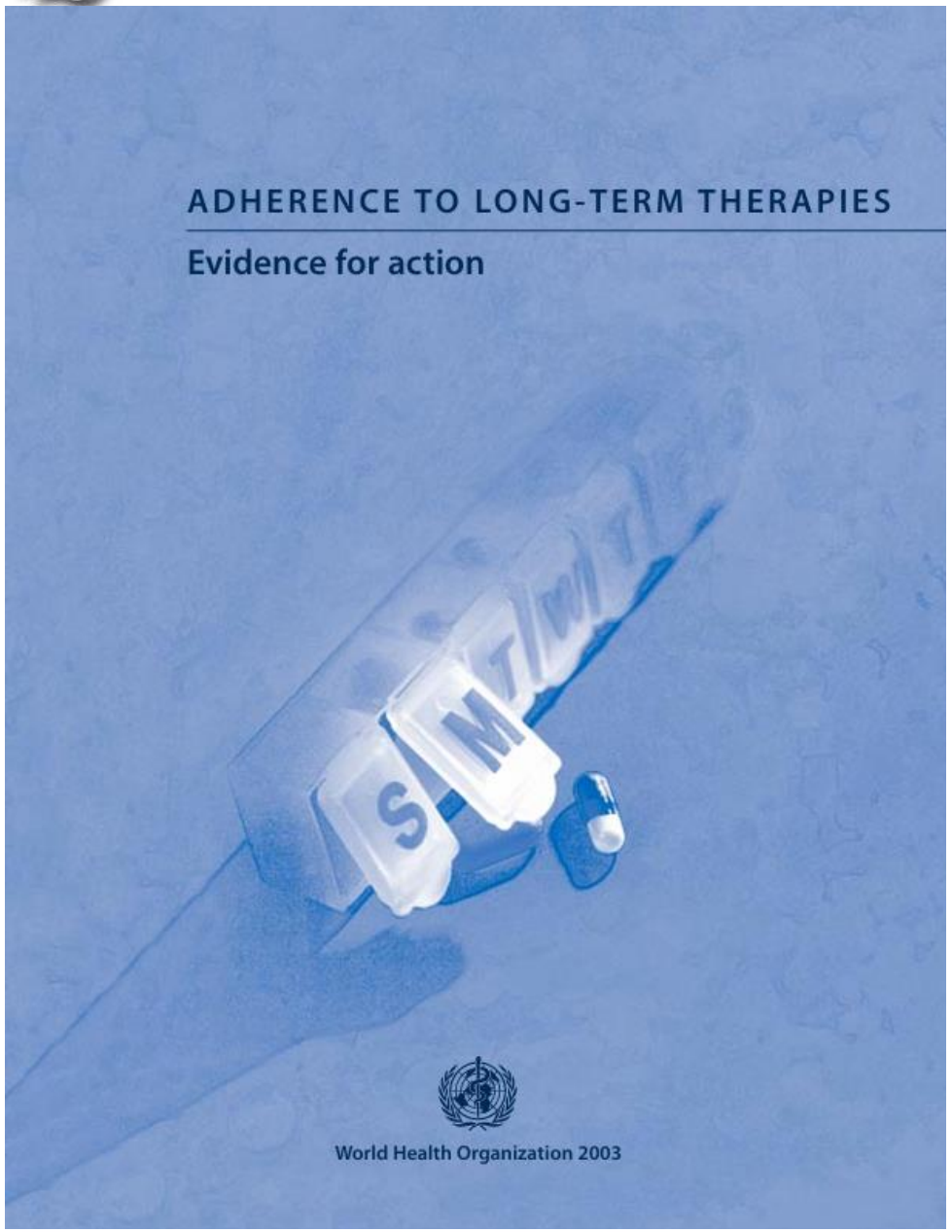
OSSERVATORIO NAZIONALE SULL'IMPIEGO DEI MEDICINALI

Indicatori di alta aderenza al trattamento con farmaci antipertensivi nella popolazione di eta ≥45 anni stratificati per sesso



Indicatori di alta aderenza al trattamento con farmaci ipolipemizzanti nella popolazione di eta ≥45 anni stratificati per sesso




ADHERENCE TO LONG-TERM THERAPIES
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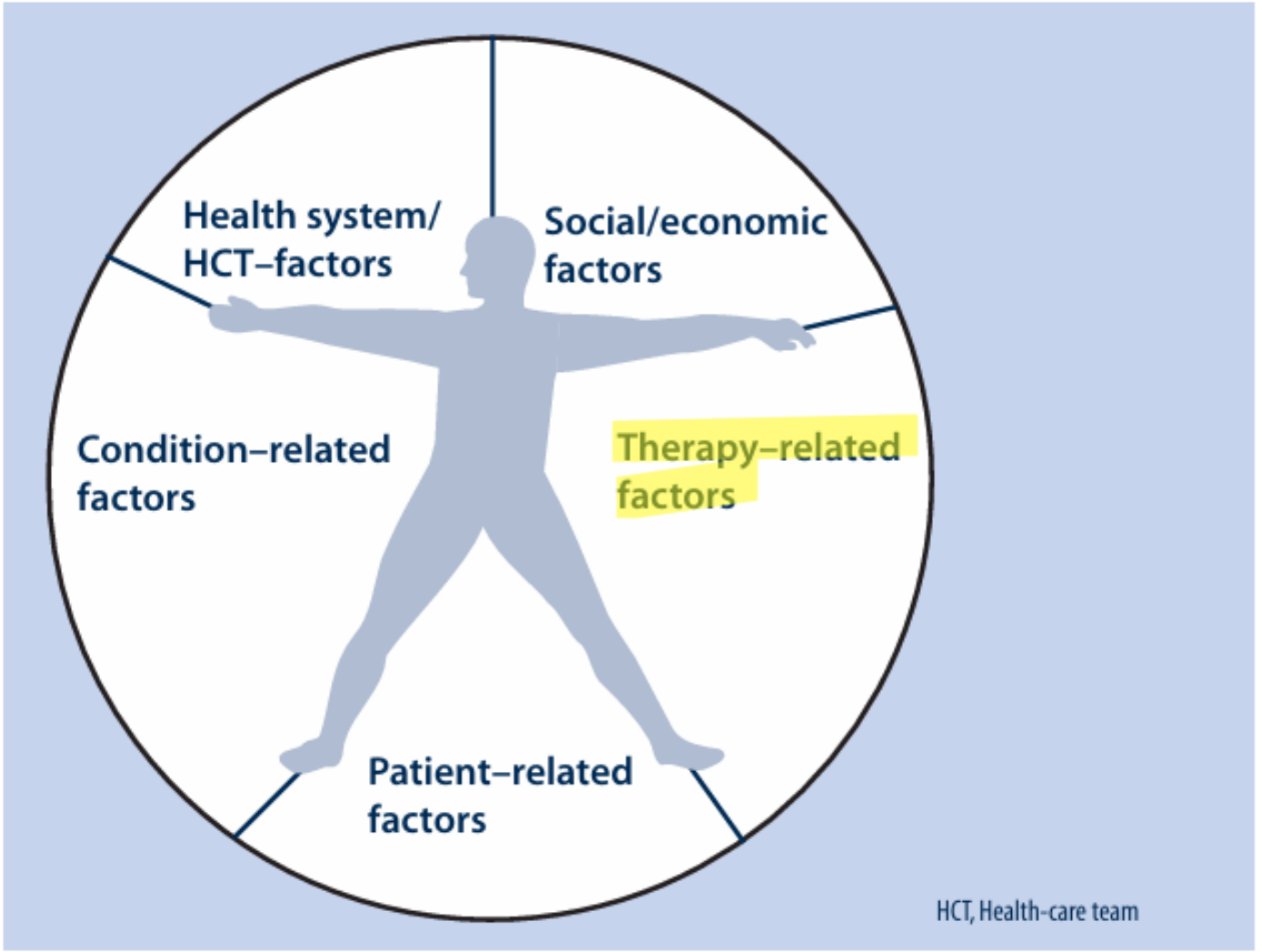
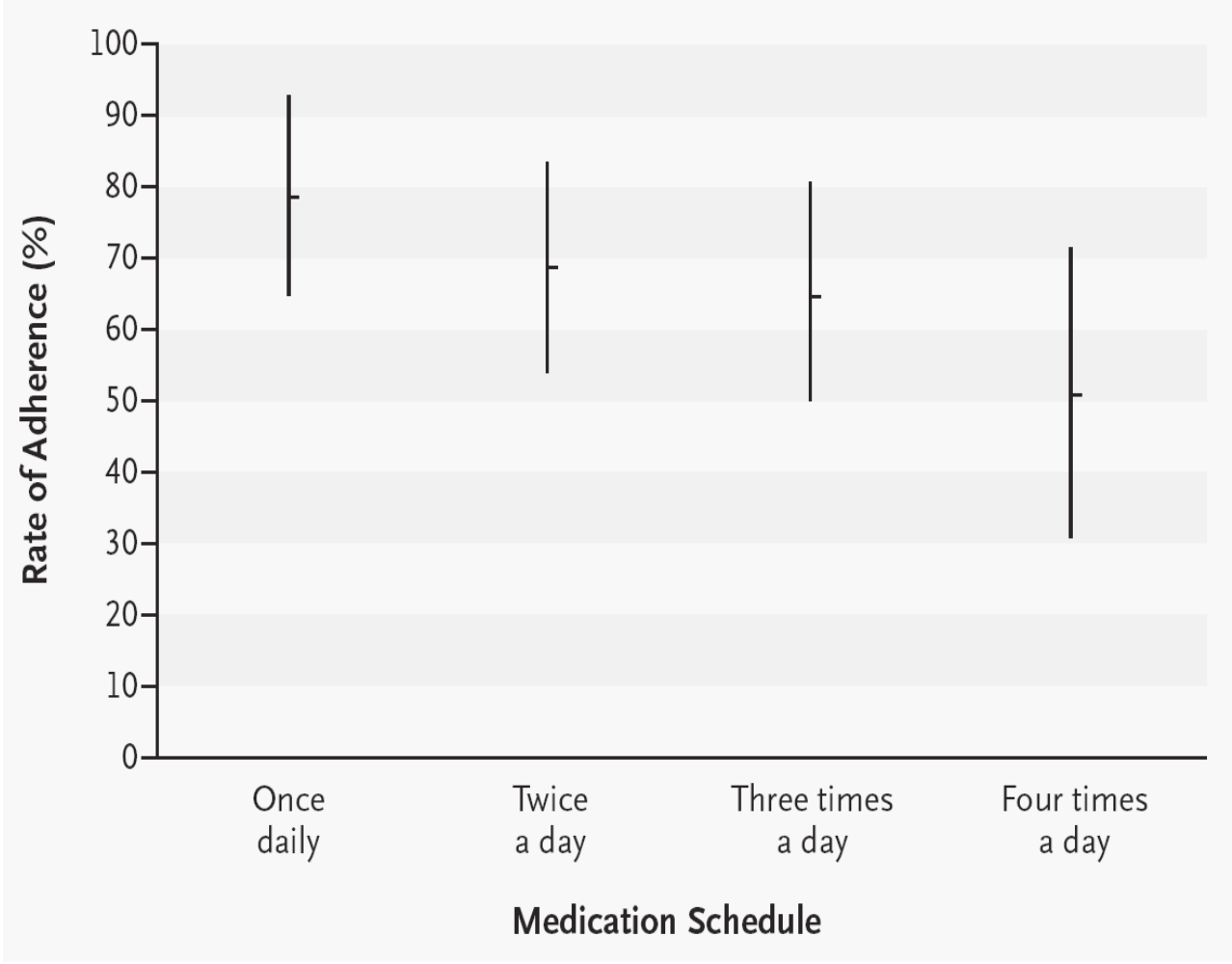
World Health Organization 2003

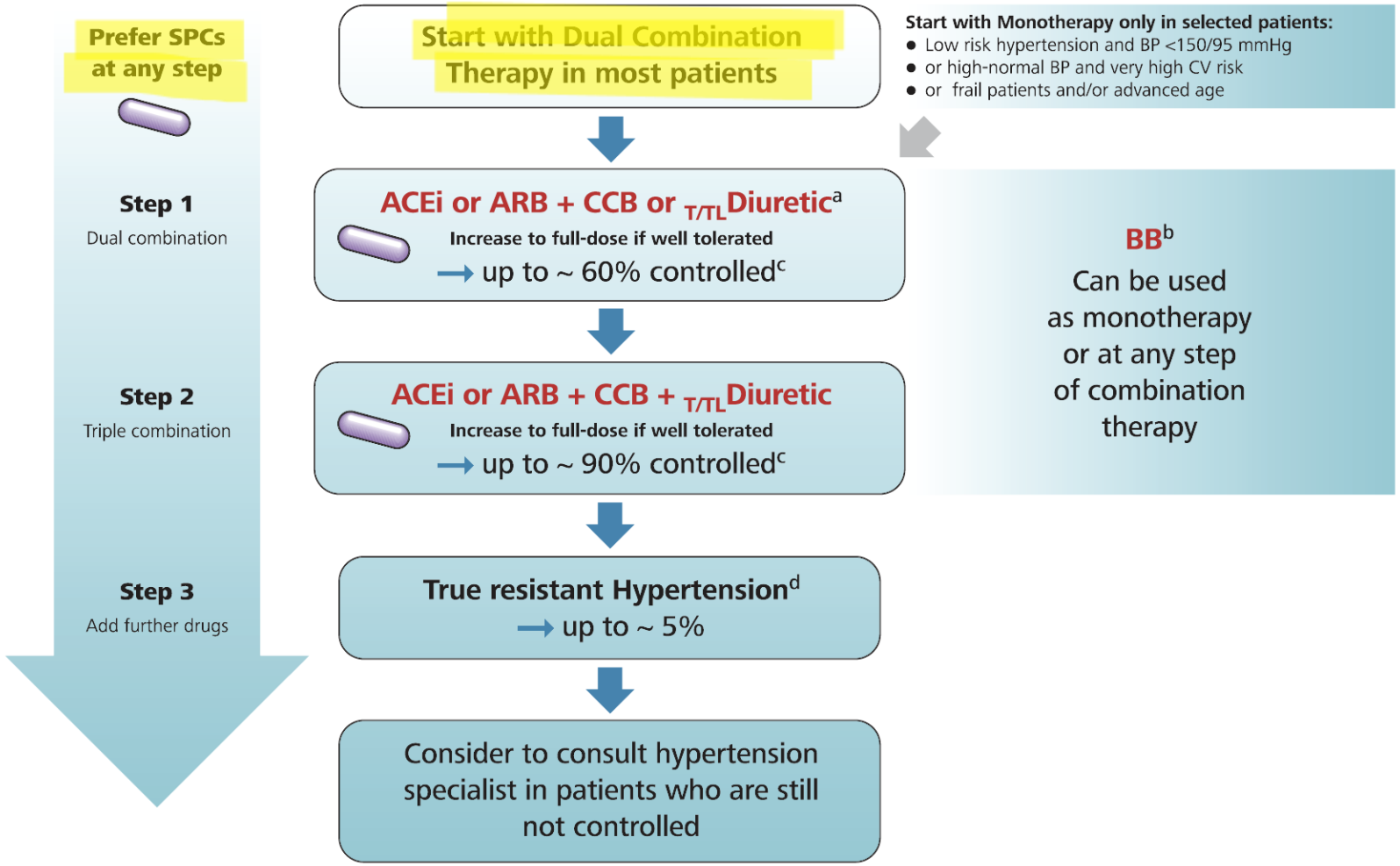

Health system/
HCT–factors
Social/economic
factors
Condition–related
factors
Therapy–related
factors
Patient–related
factors
HCT, Health-care team

First: simplicity



N Engl J Med 2005;353:487-97

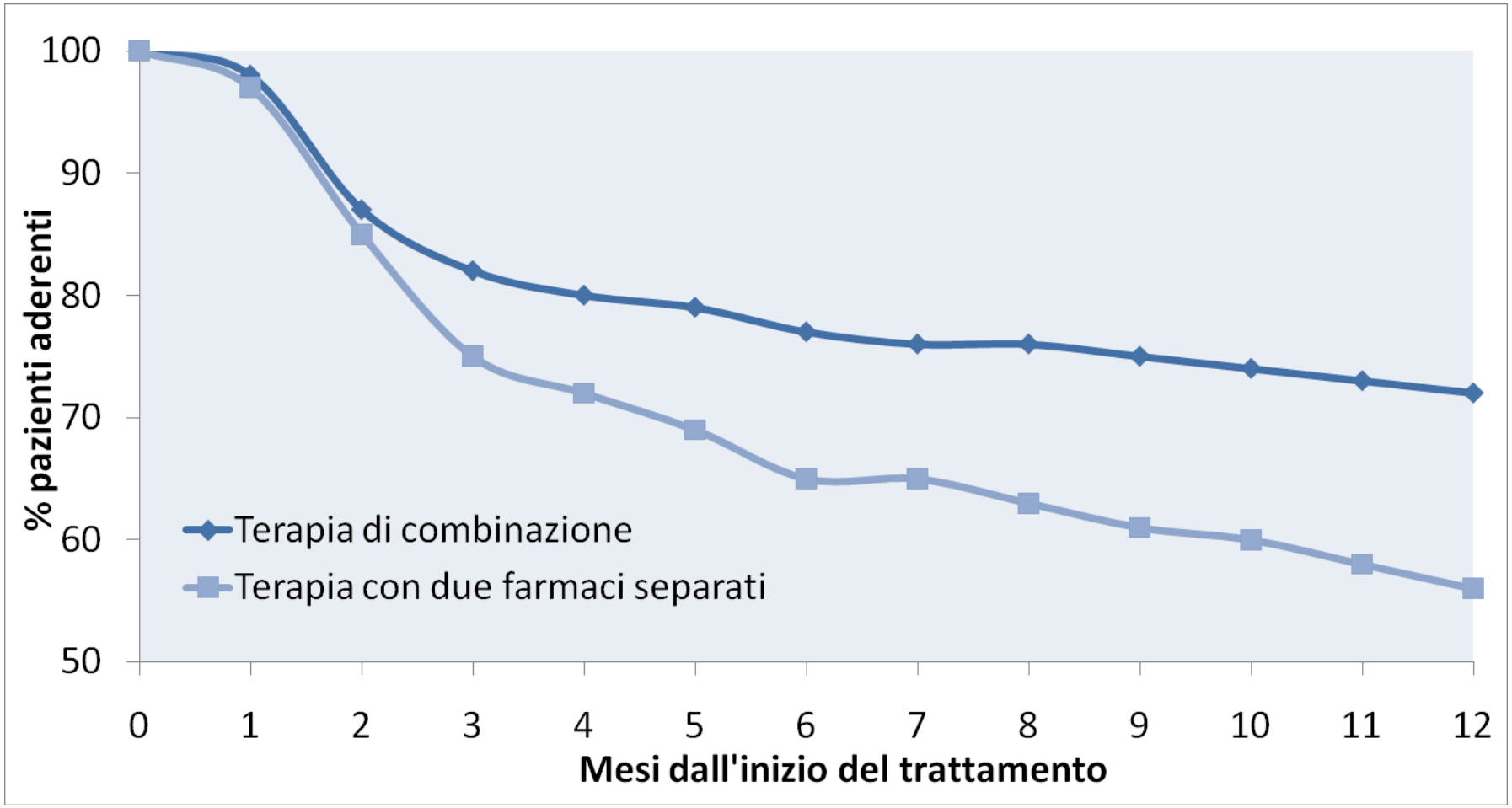
Core drug-treatment strategy for hypertension



Mancia G et al 2023 ESH Guidelines, J Hypertens, 2023

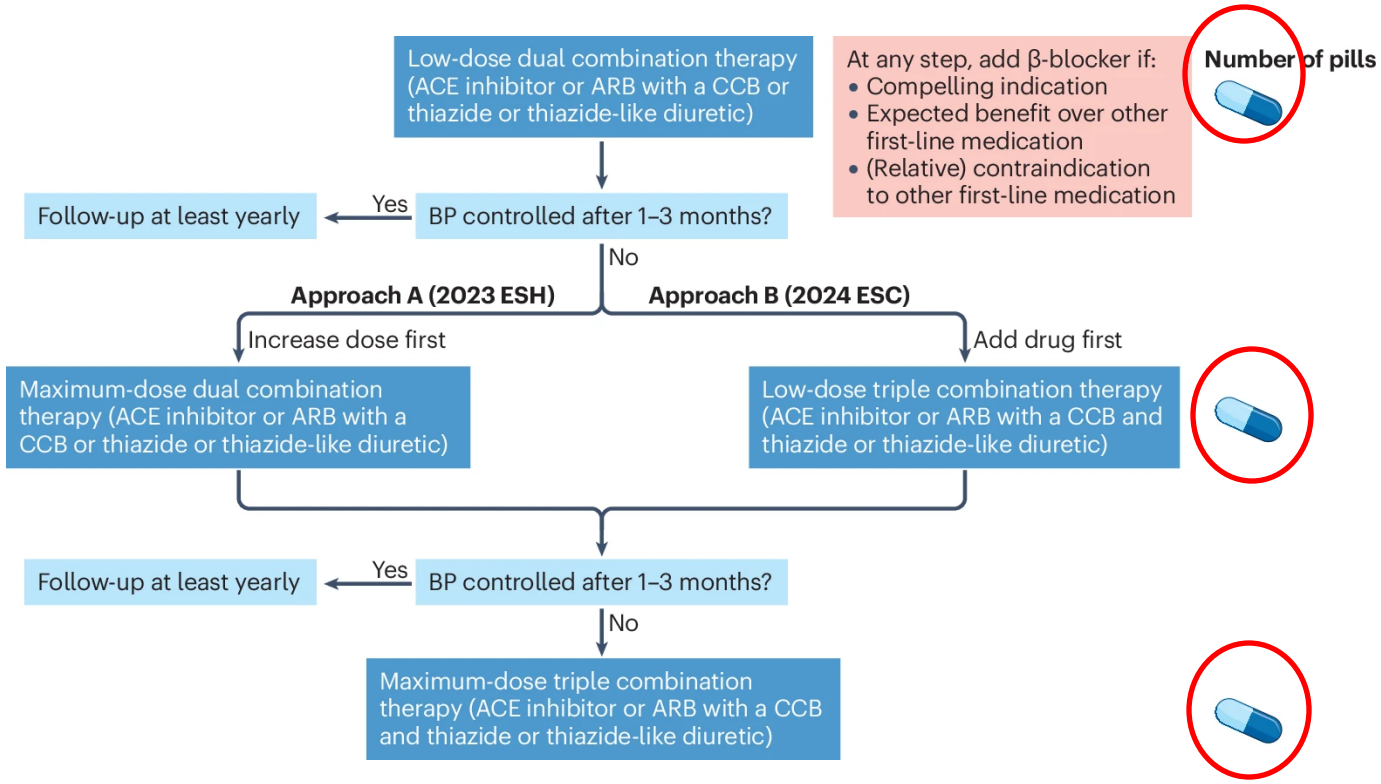
Van Vark LC et al. Eur Heart J 2012

Uno schema posologico più semplice migliora la continuità della terapia



Dezii CM. Manag Care 2000;9 (suppl):S2-S6

Il ruolo decisivo e riconosciuto della terapia di Combinazione Fissa



IPERTENSIONE

Introduzione di FDC e la loro diffusione su larga scala (2023-2050)

29

Milioni di Morti evitati

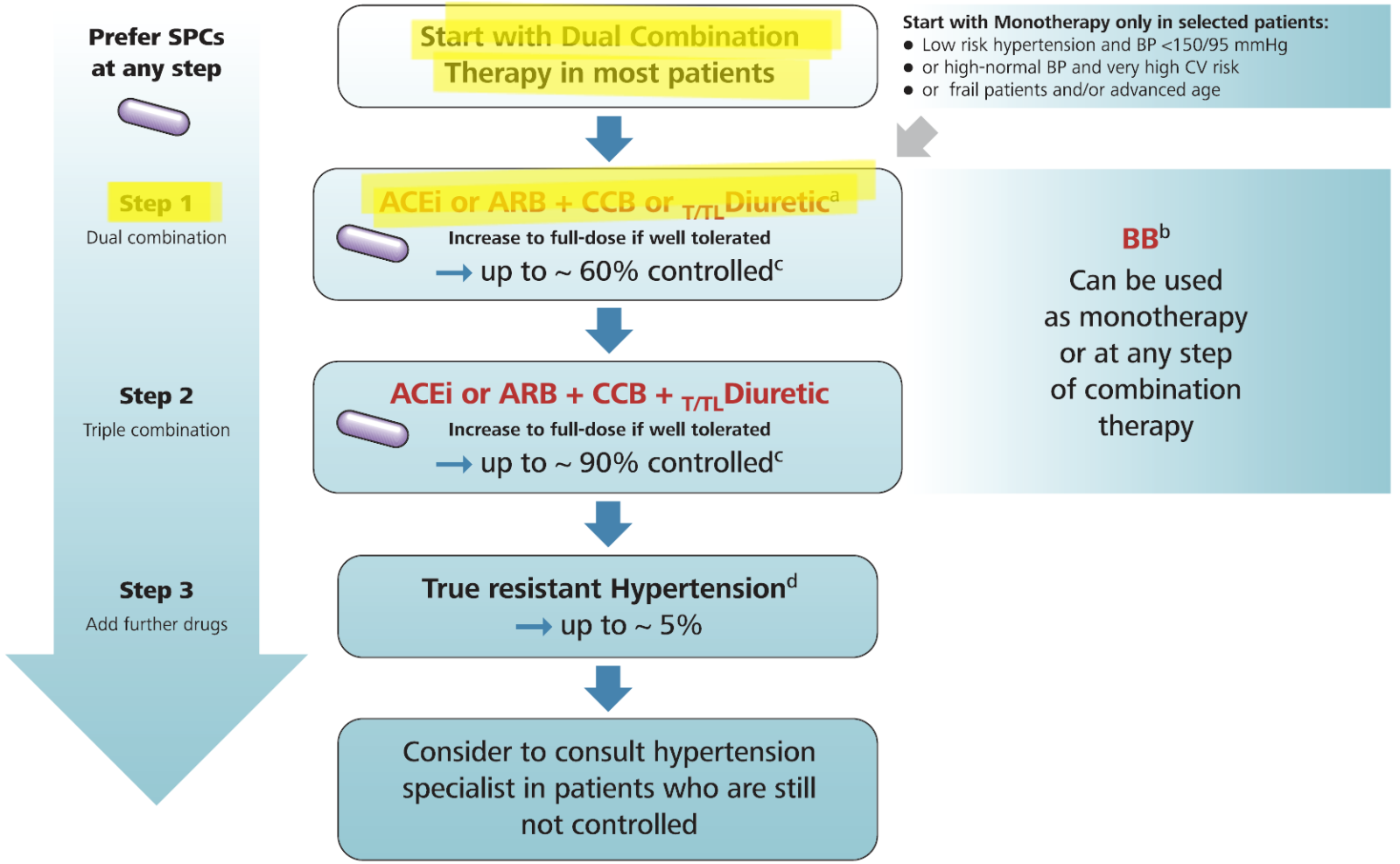
72

Milioni di Eventi Non fatali evitati

Lauder L, et al. Nat Rev Cardiol. 2025

Watkins DA, et al. JACC. 2025;86(3):149–161

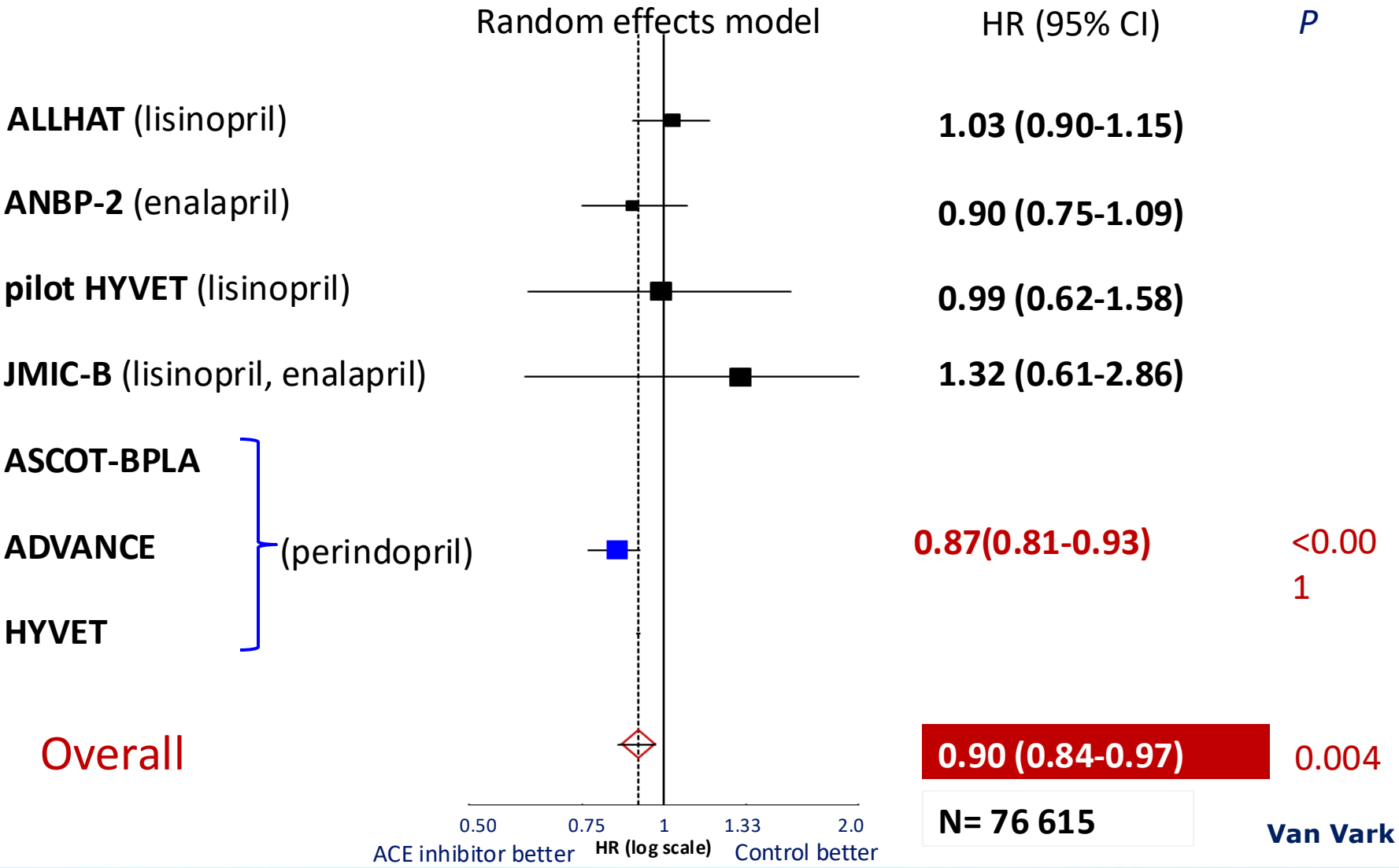
Core drug-treatment strategy for hypertension



Mancia G et al 2023 ESH Guidelines, J Hypertens, 2023

Van Vark LC et al. Eur Heart J 2012

All-cause mortality: effect of ACE inhibitors

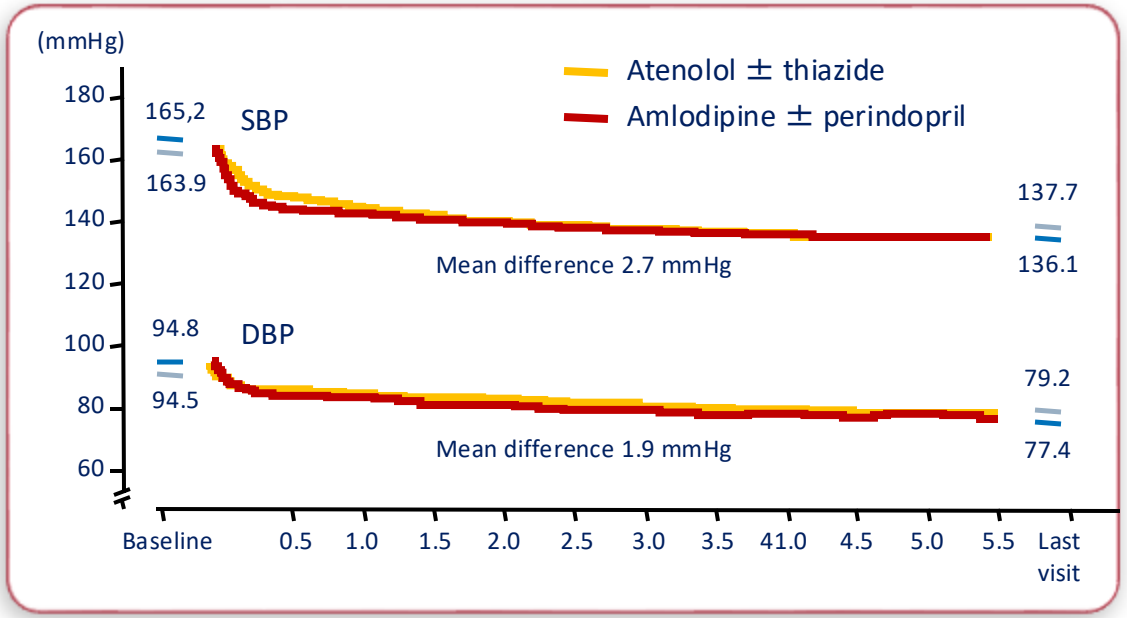


Van Vark LC et al. Eur Heart J 2012

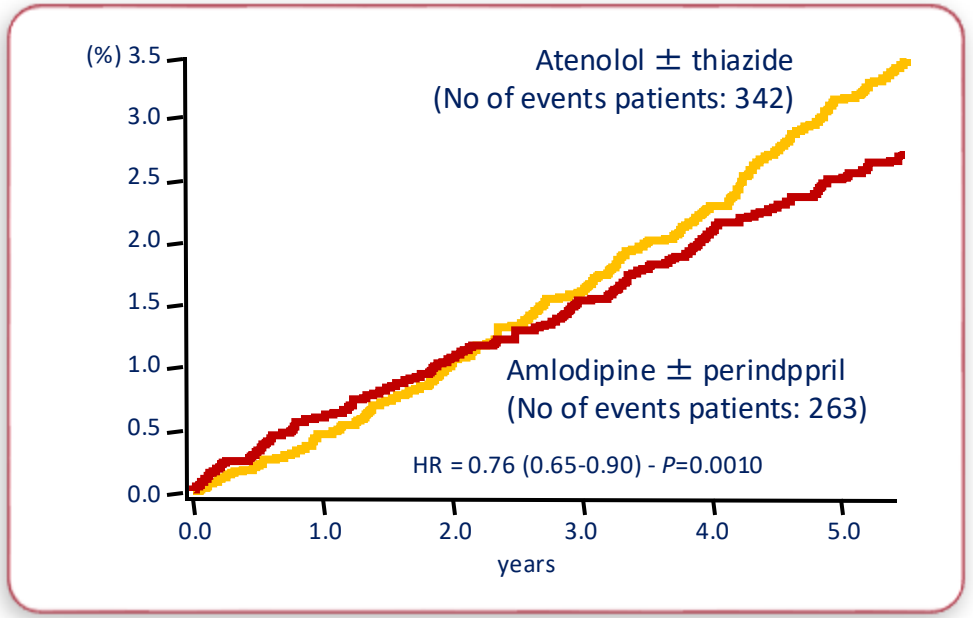
Benefit of Amlodipine/Perindopril combination in the ASCOT study

ascot

Systolic and diastolic blood pressure

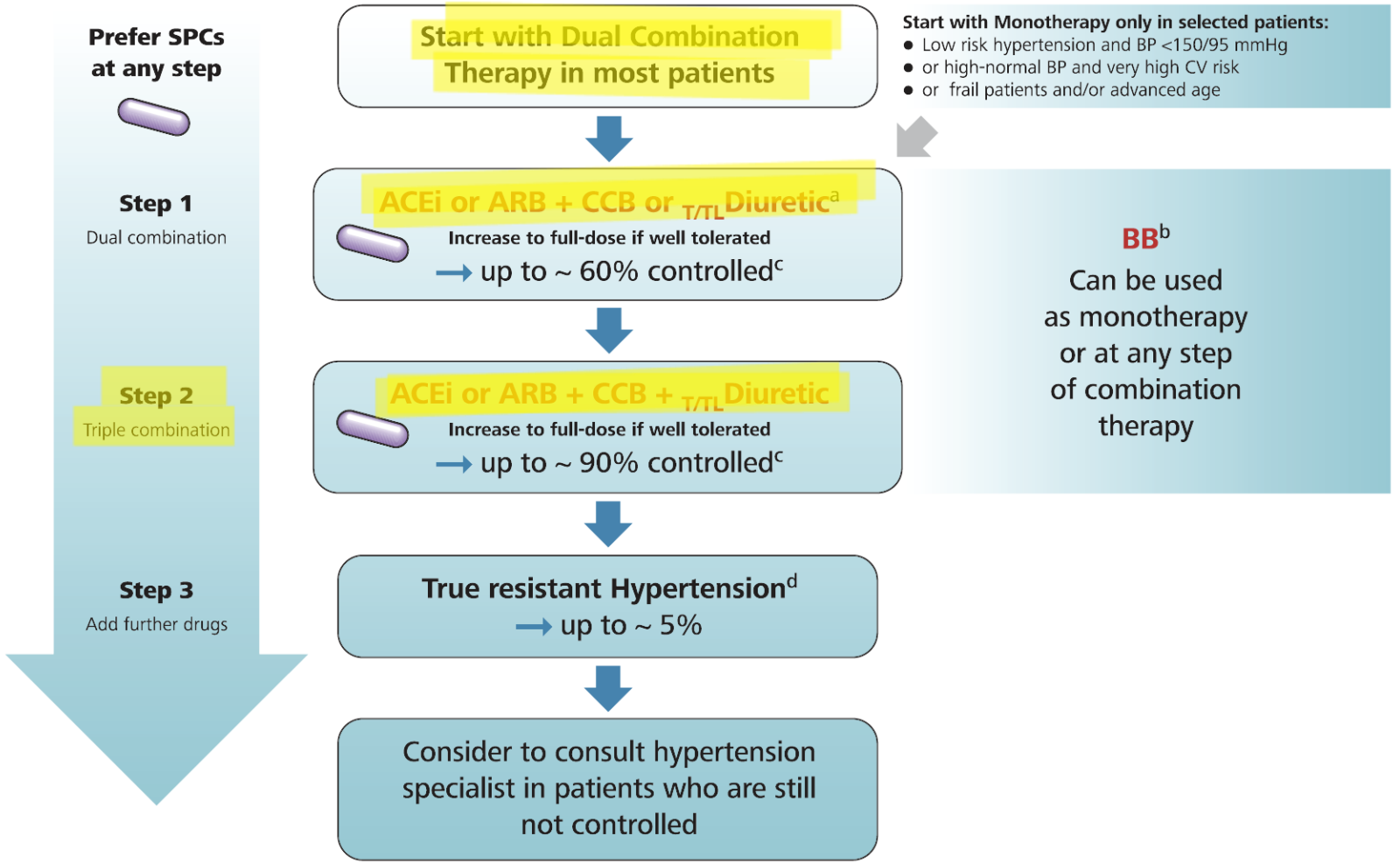


CV mortality



Dahlöf B et al. *Lancet.* 2005:366;895-906

Core drug-treatment strategy for hypertension



Mancia G et al 2023 ESH Guidelines, J Hypertens, 2023

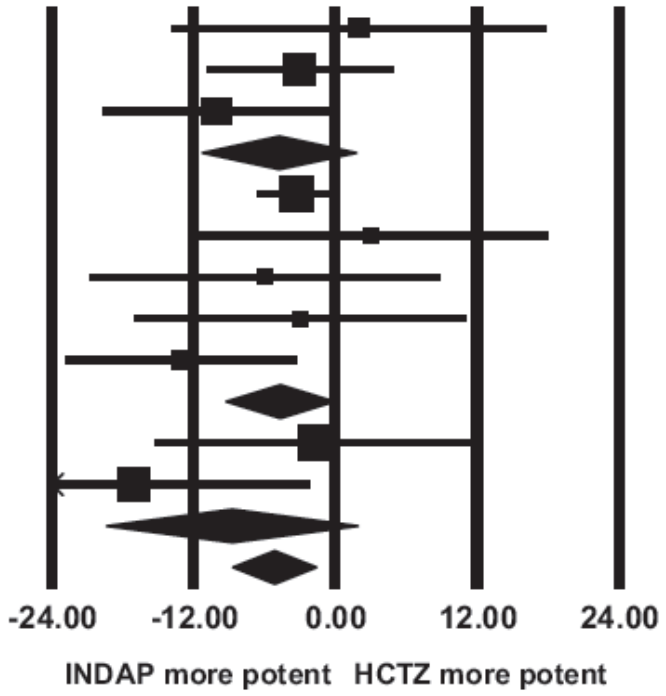
Van Vark LC et al. Eur Heart J 2012

Meta-analysis comparing the BP lowering effect of hydrochlorothiazide and indapamide in patients with HTN

Group by Dose Level	Study name	Difference in means	Lower limit	Upper limit	p-Value
Dose Equivalent	Elliott	2.000	-13.680	17.680	0.803
Dose Equivalent	Malini	-3.000	-10.785	4.785	0.450
Dose Equivalent	Spence	-10.050	-19.642	-0.458	0.040
Dose Equivalent		-4.744	-11.254	1.767	0.153
HCTZ Higher	Emeriau	-3.300	-6.542	-0.058	0.046
HCTZ Higher	Kreeft	3.000	-11.987	17.987	0.695
HCTZ Higher	Madkour	-6.000	-20.743	8.743	0.425
HCTZ Higher	Plante a	-3.000	-16.960	10.960	0.674
HCTZ Higher	Plante b	-13.000	-22.705	-3.295	0.009
HCTZ Higher		-4.657	-9.225	-0.089	0.046
INDAP Higher	Krum	-1.600	-15.146	11.946	0.817
INDAP Higher	Radevski	-17.000	-31.761	-2.239	0.024
INDAP Higher		-8.717	-19.345	1.910	0.108
Overall		-5.130	-8.657	-1.602	0.004

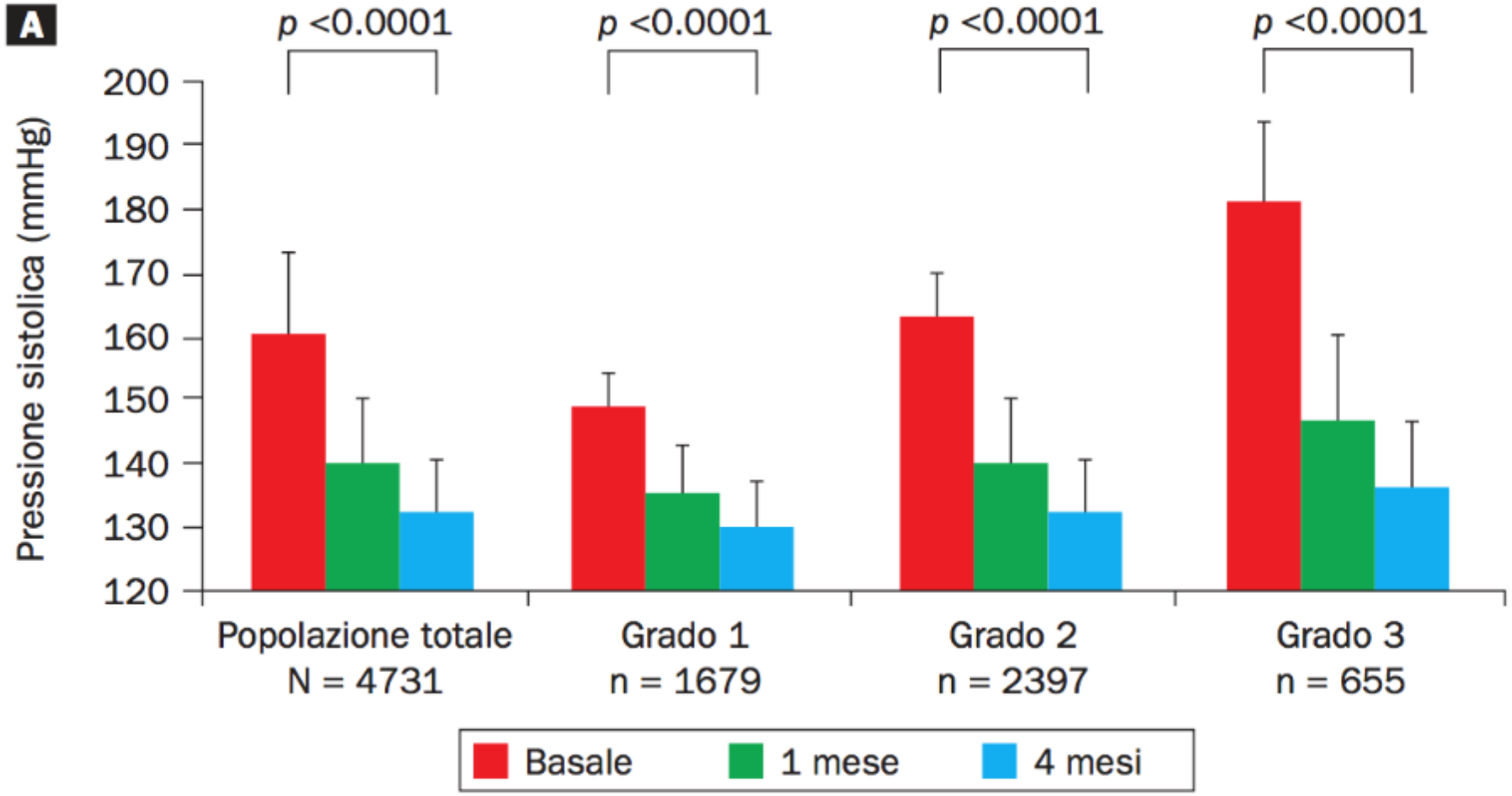
Statistics for each study

Difference in means and 95% CI



Roush G. et al. Hypertension. 2015; 65: 1041-6

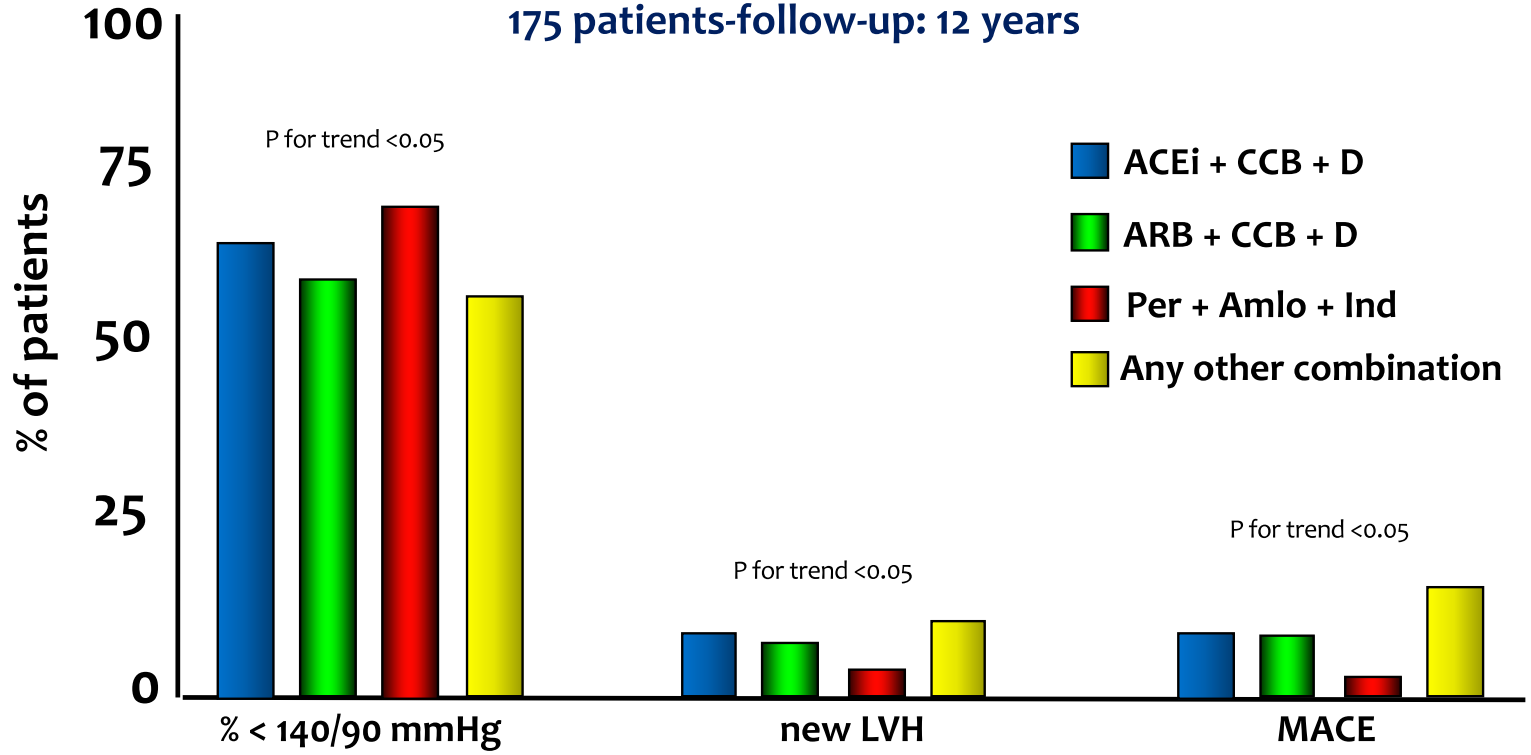
Riduzione della pressione arteriosa sistolica con la triplice combinazione perindopril/ indapamide/ amlodipina in ipertesi a rischio elevato o molto elevato: studio PIANIST



Tóth K et al. Am J Cardiovasc Drugs. 2014;14:137-45

Long-Term impact of different triple combination antihypertensive medications on blood pressure control, metabolic pattern and incident events: data from the Brisighella Heart Study

Rate of BP control and clinical profile in hypertensive pts treated with different combination of antihypertensive drugs

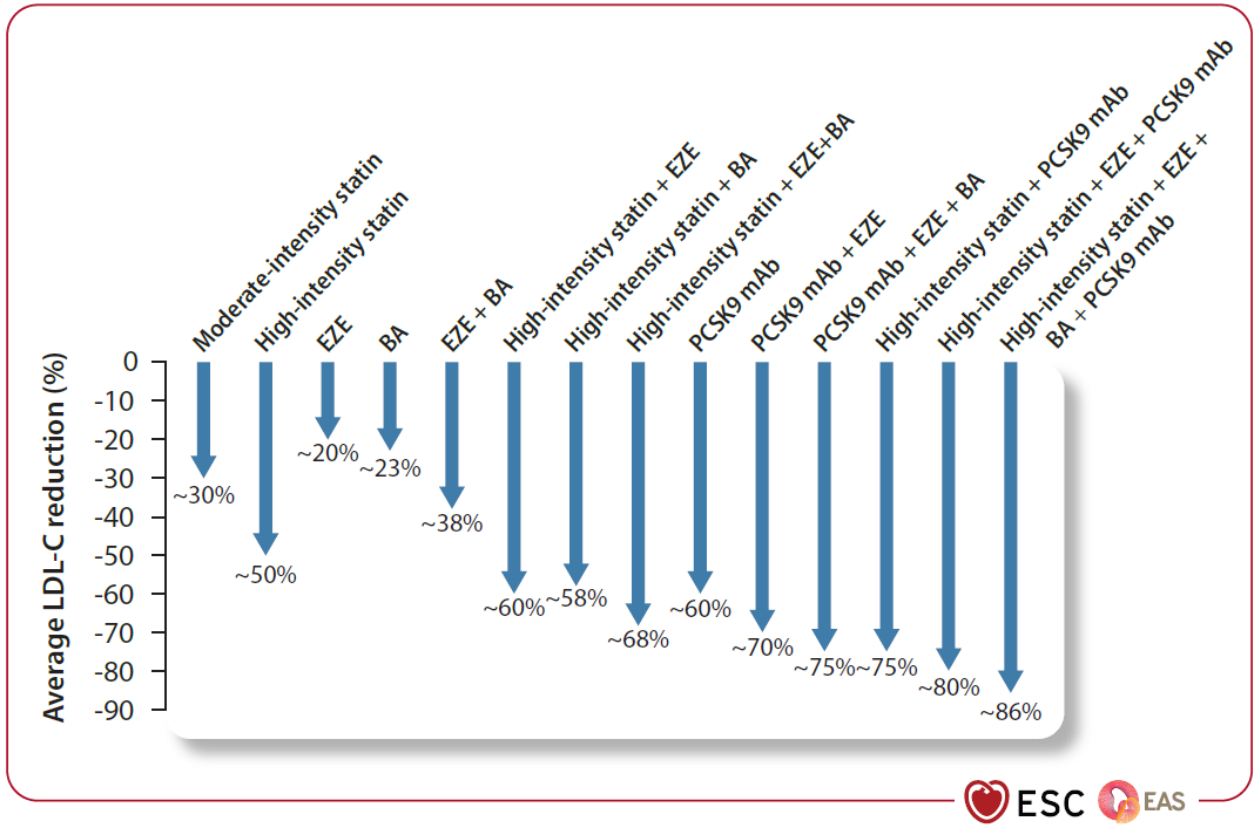


Cicero AFC et al. J Clin Med 2021

Le LG aggiornate 2025: ruolo centrale di Ezetimbe e del valore dell'associazione con statina

ESC European Society of Cardiology

EAS



Recommendation Table 3 — Recommendations for lipid-lowering therapy in patients with acute coronary syndromes (see also Supplementary data online, Evidence Table 3)

Recommendations	Class[a]	Level[b]
Intensification of lipid-lowering therapy during the index ACS hospitalization is recommended for patients who were on any lipid-lowering therapy before admission in order to further lower LDL-C levels.	I	C
Initiating combination therapy with high-intensity statin plus ezetimibe during index hospitalization for ACS should be considered in patients who were treatment-naïve and are not expected to achieve the LDL-C goal with statin therapy alone.[66]	IIa	B

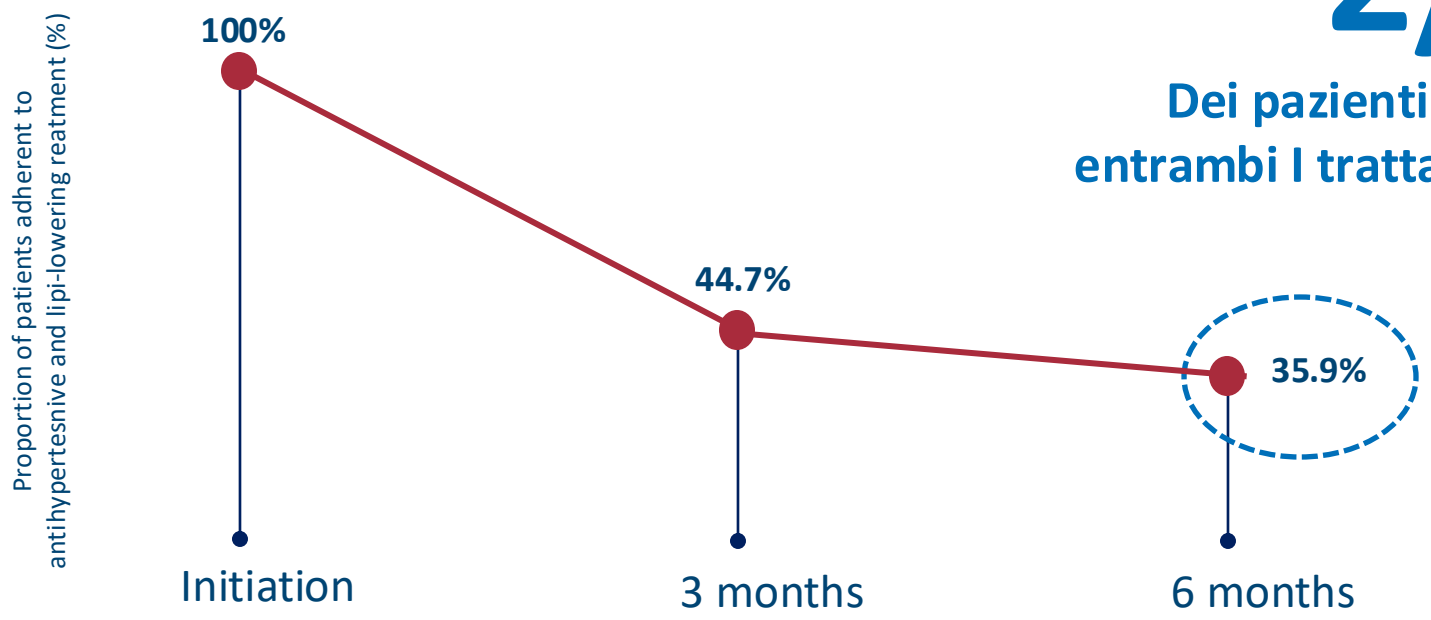
ROSUVASTATIN + EZETIMIBE: DUAL LIPID MANAGEMENT IN ONE PILL

Improved Lipid Profile Vs Statin monotherapy [7]	Enhanced Anti-inflammatory Effects	Greater Atheroma Regression Vs. Rosuvastatin	Reduction on Cardiovascular Outcomes (Vs Statin alone)
○ **LDL-C:** −43% ○ **Non–HDL-C:** −36% ○ **ApoB:** −24% ○ **Total-C:** −23% ○ **Triglycerides:** −12%	**−78%** hsCRP and **−59%** IL-6 at 12 months with ezetimibe + rosuvastatin vs baseline. significantly outperforming rosuvastatin alone in reducing systemic inflammation.	The combination therapy shrinks the plaque **−15,36%** plaque burden, **−45,83%** area **−22%** necrotic core (makes it more stable).	↓**19%** in All-Cause Mortality (ACM). ↓ **18%** in Major Adverse Cardiovascular Events (MACE). ↓ **17%** in Stroke.

The combination of moderate-intensity rosuvastatin with ezetimibe was found to be an effective alternative to high-intensity statins, offering better efficacy and safety

E per chi ha sia ipertensione che ipercolesterolemia ?

L'aderenza al trattamento decresce nei pazienti trattati per ipercolesterolemia e ipertensione



2/3

Dei pazienti interrompono entrambi I trattamenti dopo 6 mesi

Chapman RH et al. Arch Intern Med. 2005;165:1147-1152

Special Report

The Polypill in the Prevention of Cardiovascular Diseases

Key Concepts, Current Status, Challenges, and Future Directions

Eva Lonn, MD, MSc; Jackie Bosch, MSc; Koon K. Teo, MD, PhD; Prem Pais, MD; Denis Xavier, MD; Salim Yusuf, MBBS, DPhil

Circulation. 2010;122:2078-2088

The Concept of the Polypill in the Prevention of Cardiovascular Disease

Annals of Global Health 2014;80:24-34

Brandon Wiley, MD, and Valentin Fuster, MD, PhD

DEBATE Open Access

The polypill approach – An innovative strategy to improve cardiovascular health in Europe

Valentín Fuster[1,2], Francesc Gambús[3], Aldo Patriciello[4], Margaretha Hamrin[5] and Diederick E. Grobbee[6]

Fuster et al. BMC Pharmacology and Toxicology 2017; 18:10

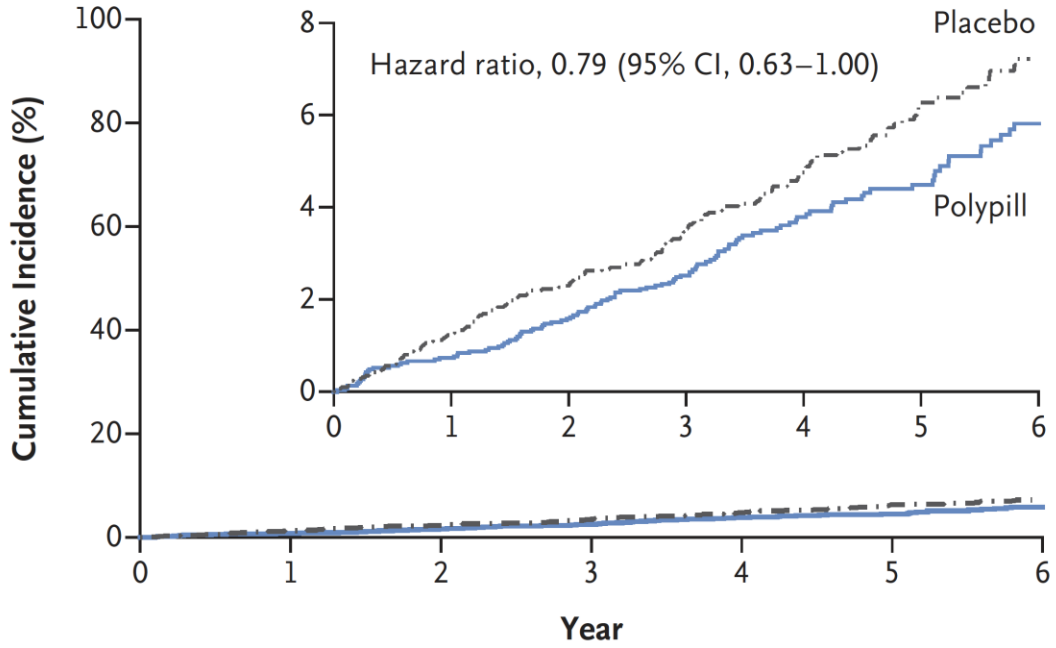
ORIGINAL ARTICLE

Polypill with or without Aspirin in Persons without Cardiovascular Disease

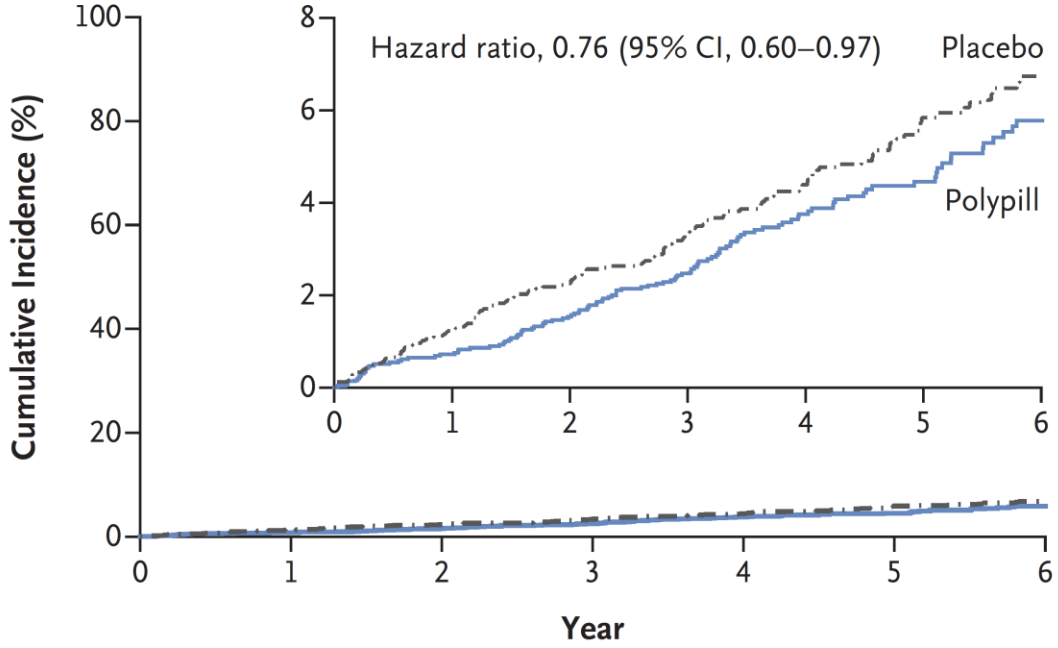
S. Yusuf, P. Joseph, A. Dans, P. Gao, K. Teo, D. Xavier, P. López-Jaramillo, K. Yusoff, A. Santoso, H. Gamra, S. Talukder, C. Christou, P. Girish, K. Yeates, F. Xavier, G. Dagenais, C. Rocha, T. McCready, J. Tyrwhitt, J. Bosch, and P. Pais, for the International Polycap Study 3 Investigators*

40 mg of simvastatin
100 mg of atenolol
25 mg of hydrochlorothiazide
10 mg of ramipril

A First Event of the Primary Outcome



B First and Recurrent Events of the Primary Outcome



Yusuf S et al. N Engl J Med 2021;384:216-28

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ESTABLISHED IN 1812 SEPTEMBER 15, 2022 VOL. 387 NO. 11

Polypill Strategy in Secondary Cardiovascular Prevention

J.M. Castellano, S.J. Pocock, D.L. Bhatt, A.J. Quesada, R. Owen, A. Fernandez-Ortiz, P.L. Sanchez, F. Marin Ortuño, J.M. Vazquez Rodriguez, A. Domingo-Fernández, I. Lozano, M.C. Roncaglioni, M. Baviera, A. Foresta, L. Ojeda-Fernandez, F. Colivicchi, S.A. Di Fusco, W. Doehner, A. Meyer, F. Schiele, F. Ecarnot, A. Linhart, J.-C. Lubanda, G. Barczi, B. Merkely, P. Ponikowski, M. Kasprzak, J.M. Fernandez Alvira, V. Andres, H. Bueno, T. Collier, F. Van de Werf, P. Perel, M. Rodriguez-Manero, A. Alonso Garcia, M. Proietti, M.M. Schoos, T. Simon, J. Fernandez Ferro, N. Lopez, E. Beghi, Y. Bejot, D. Vivas, A. Cordero, B. Ibañez, and V. Fuster, for the SECURE Investigators*

N=2500 Post MI >65

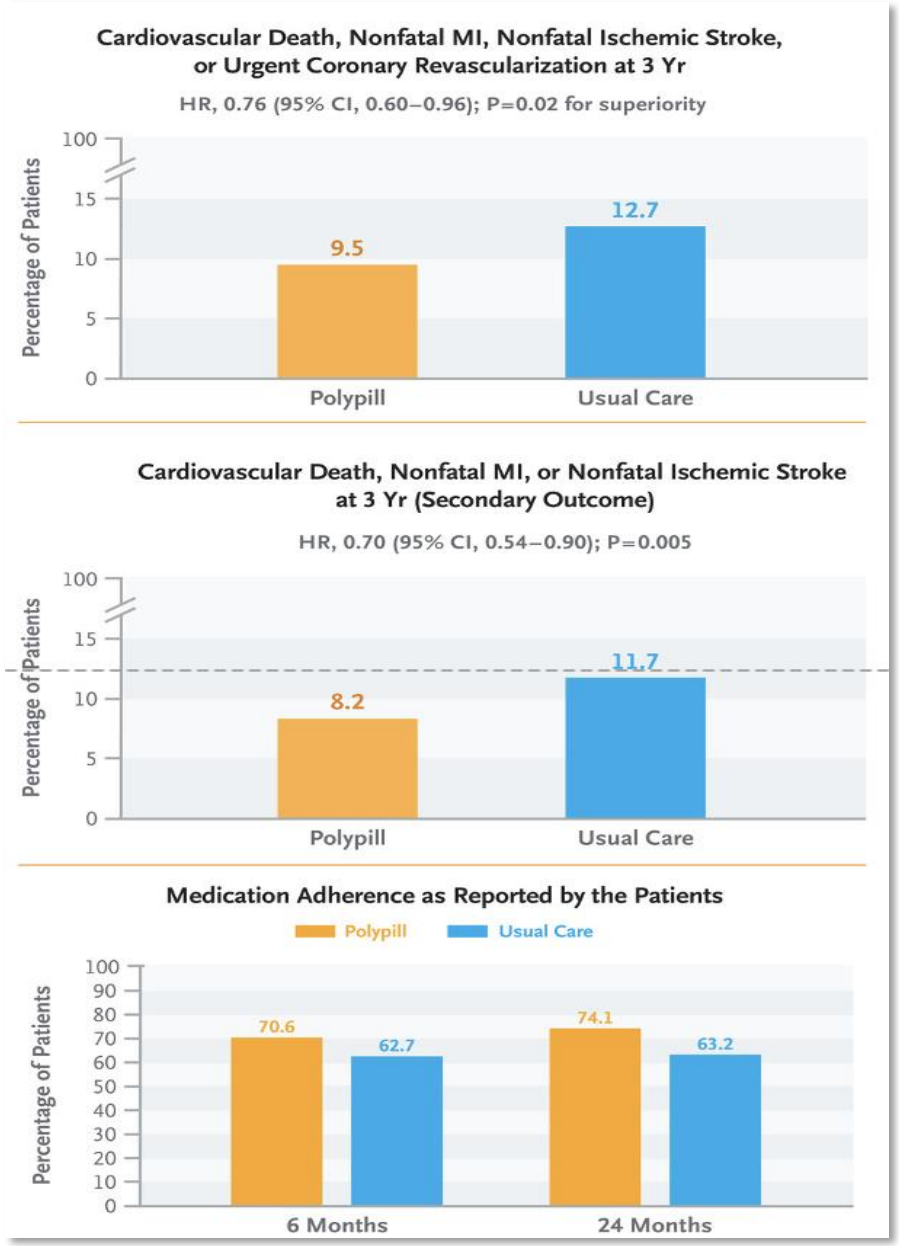
ASA 100
ATORVASTATIN 20/40
RAMIPRIL 2.5/5/10

+ At Least One

a. Documented DM
b. Mild to moderate CKD
c. Prior MI
d. Prior coronary revascularization
e. Prior stroke
f. Age ≥ 75 years

Median FU: 3 years

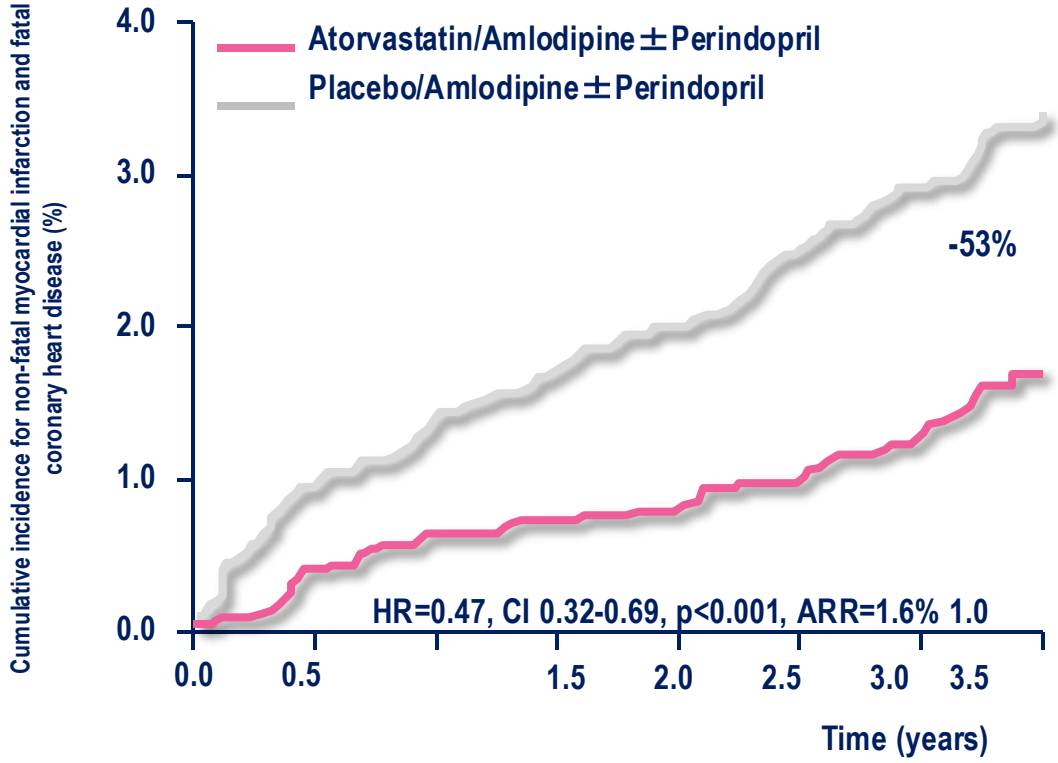
The primary composite endpoint
cardiovascular death, MI, stroke, or urgent revascularization.
The key secondary endpoint
cardiovascular death, MI, or stroke.

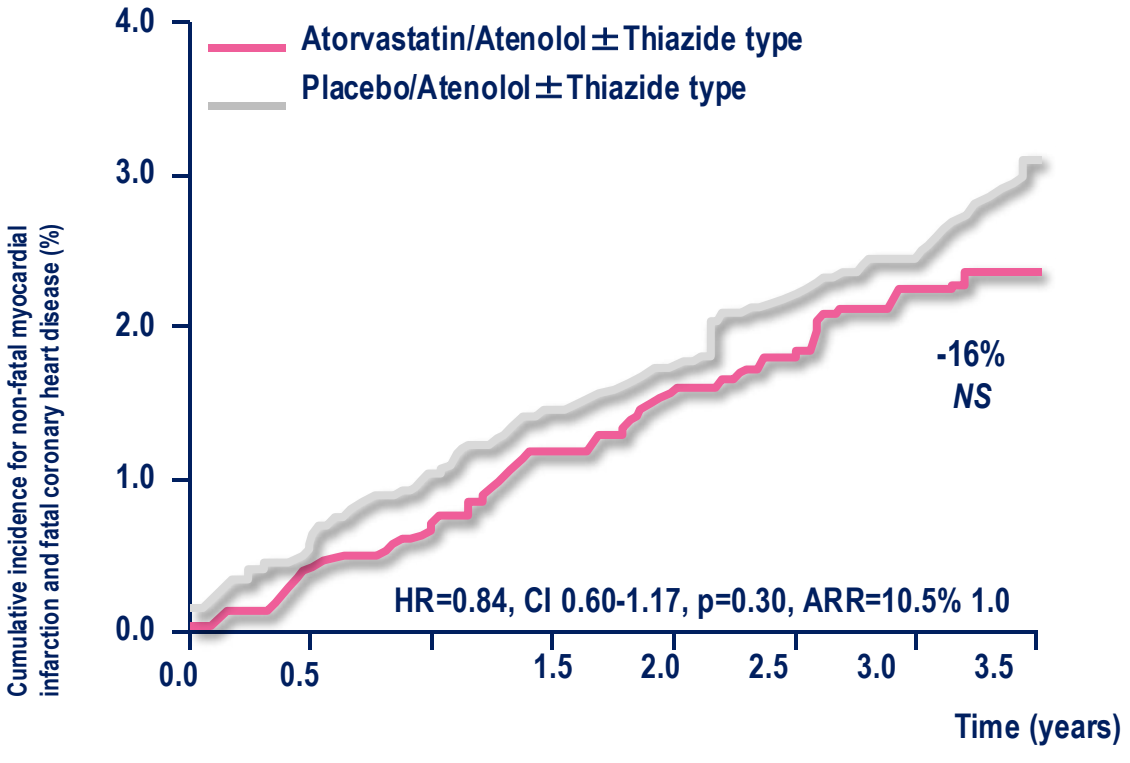


Castellano JM et al. N Engl J Med 2022;387:967-77

Synergy between atorvastatin, amlodipine and perindopril for CV protection

ASCOT-LLA, RCT: n=10,305 hypertensive patients with at least 3 cardiovascular risk factors and total cholesterol ≤6.5 mmol/L. Follow-up 3.3 years





Sever et al. Eur Heart J. 2006;27:2982-2988

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EDITOR'S PAGE

Problems With Immortality

Anthony N. DeMaria, MD
Editor-in-Chief, Journal of the American College of Cardiology

Although immortality is, I guess, one of the ultimate goals of medicine, no human has thus far achieved it, nor is anyone likely to do so for the foreseeable future. However, the same is not true for human tissue. I recently read a book about Henrietta Lacks (1), the woman whose cancer provided the HeLa cell line that has thus far proved immortal and has been responsible for many fundamental scientific breakthroughs. Although these cells and the discoveries they have enabled are a cause for celebration, they have also been representative of a number of problematic issues in medicine, many of which remain unresolved. In fact, some of the issues may be even more prominent today as we strive to develop stem cells and achieve tissue regeneration.

Henrietta Lacks was a poor African-American woman living in Baltimore who developed a very malignant carcinoma of the cervix at a young age. The cells from this tumor were taken, for all intents and purposes without her knowledge or consent, and sent for possible tissue culture at Johns Hopkins University. They proved to be the first "immortal" human cells capable of forever continuously reproducing when cultured outside of the body, enabled many medical advances, and also became a profitable commercial product. Today, HeLa cells can be found in laboratories throughout the world, and they continue to be the cornerstone of a large body of medical research.

The first aspect of the HeLa story that struck me, as it might most clinical investigators, was the serendipity of discovery. George Gey, the Hopkins researcher who grew the cells, had been unsuccessfully trying to culture human cells for many years. He had experimented with a myriad of culture media recipes without success. In fact, there was nothing unique or special about the media in which he placed Henrietta Lacks' cells in comparison to that used for many other cells that did not reproduce. The "discovery" was the result of the good fortune of obtaining cells that were almost indestructible. It is amazing to think of how many critical medical discoveries have depended heavily upon chance. However, it is also true that luck leads to important discoveries when it encounters the prepared mind. Henrietta's cells were absolutely unique, but they would have gone undetected and unrecognized had not George Gey been looking and been irrepressible in his search.

A perhaps weightier issue regarding the HeLa story relates to the socioeconomic status of the donor. Henrietta Lacks was a poor woman with little formal education who came under the clinical care of a research medical institution that provided safety net treatment for the uninsured. Although less prevalent today, this arrangement was fairly typical of the times (1950s to 1960s). So, the lower socioeconomic classes typically contributed disproportionately to the pool of research patients. Patients were sometimes uninformed about investigation, much less asked for their consent. We have long since rejected any such notions, and many of the courageous and altruistic patients who participate at uncertain risk in clinical trials now come

Perhaps the most problematic, and still largely unresolved, issue raised by the HeLa story concerns the ownership of tissue once it is removed from the body.

Is it possible?
Is there a price to pay?

Meeting Nazionale ITACARE-P 2025

La Cardiologia Riabilitativa e Preventiva come snodo fondamentale della cura della persona con cardiopatia

CENTRO CONGRESSI FRENTANI
Roma, 21-22 novembre 2025