



Nuovi target nel trattamento dell'ipertensione arteriosa e come raggiungerli

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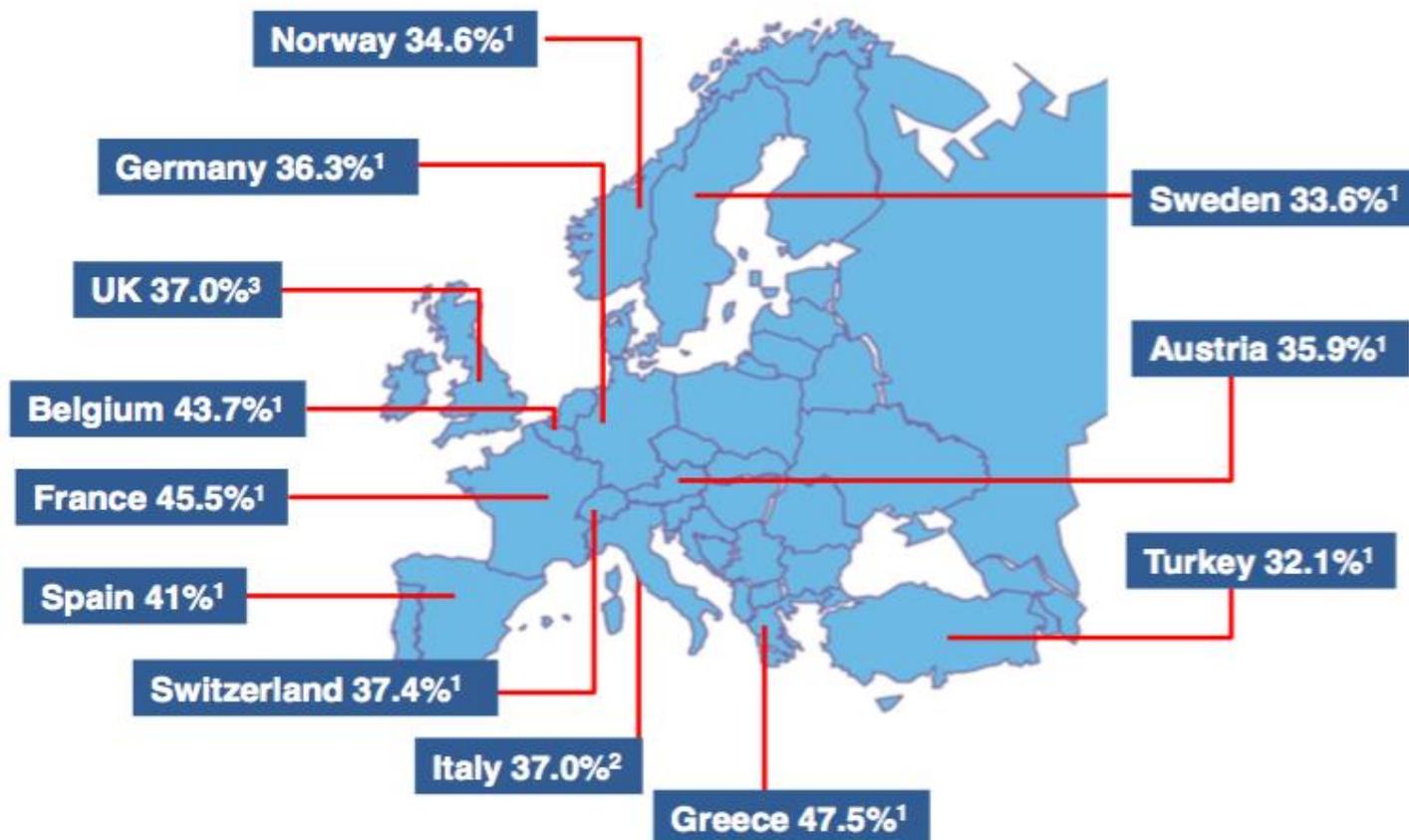
Conflict of Interest Statement

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| | |
|----------------------------------|---|
| Title | MD, Full Professor of Cardiology, FESC, FAHA |
| Current Occupation | University of Rome Sapienza, Department of Clinical and Molecular Medicine |
| Current Grants | Award University of Rome Sapienza, Member of CNGR at Ministry of University and Research, Italy |
| Speakers' Bureau | Menarini International, Daiichi-Sankyo Europe, Berlin Chemie, Bayer |
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| Other Activities | Reviewer ESH/ESC Hypertension Guidelines and ESC CV Prevention Guidelines Past-President of the Italian Society of Hypertension (SIIA) President of the Italian Society of Cardiovascular Prevention (SIPREC) |

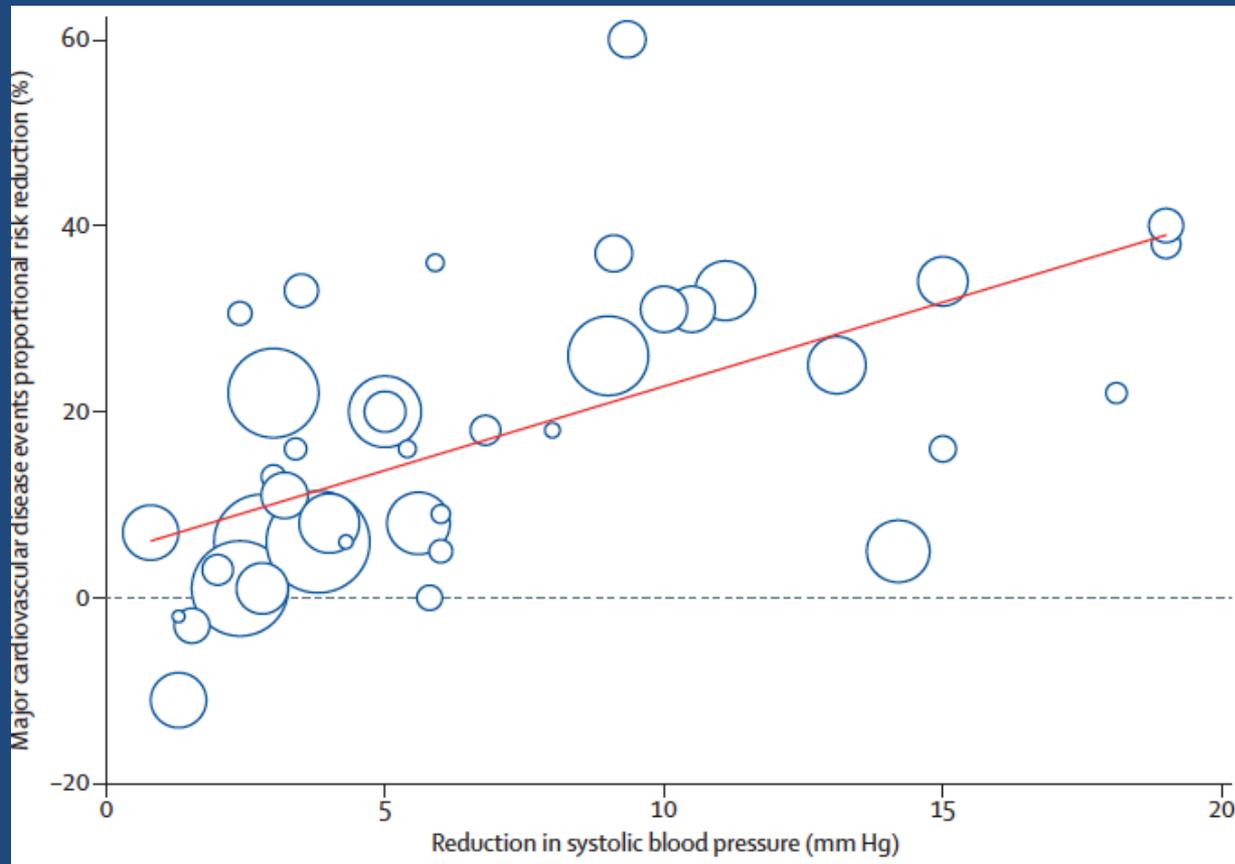
Hypertension Control in Europe



1. Proportion (%) of primary care patients with SBP/DBP <140/90 mmHg (<130/80 mmHg for diabetics)
2. Proportion (%) of patients (mainly in primary care) with SBP/DBP <140/90 mmHg

1. Banegas et al. *Eur Heart J* 2011;32:2143–522.
2. Tocci et al. *J Hypertens* 2012;30:1065–74,
3. Falaschetti et al. *Lancet* 2014;383:1912–19

Blood Pressure Reduction and Cardiovascular Disease Risk Reduction



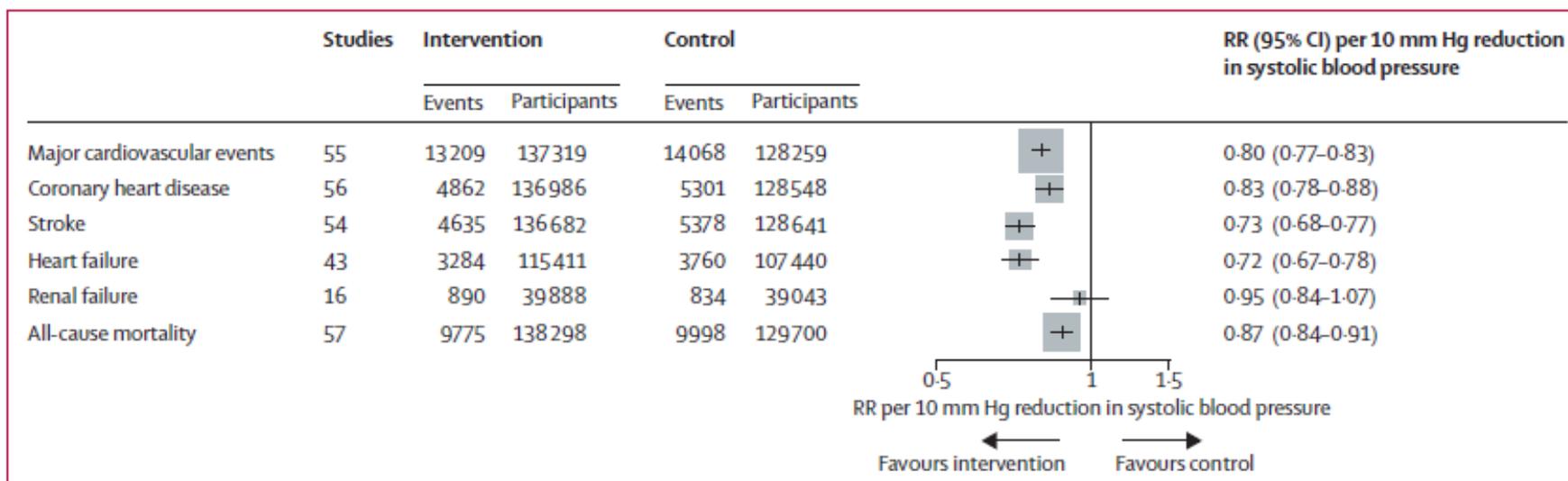
20 mmHg reduction in BP reduces CVD risk by almost 40%

Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis

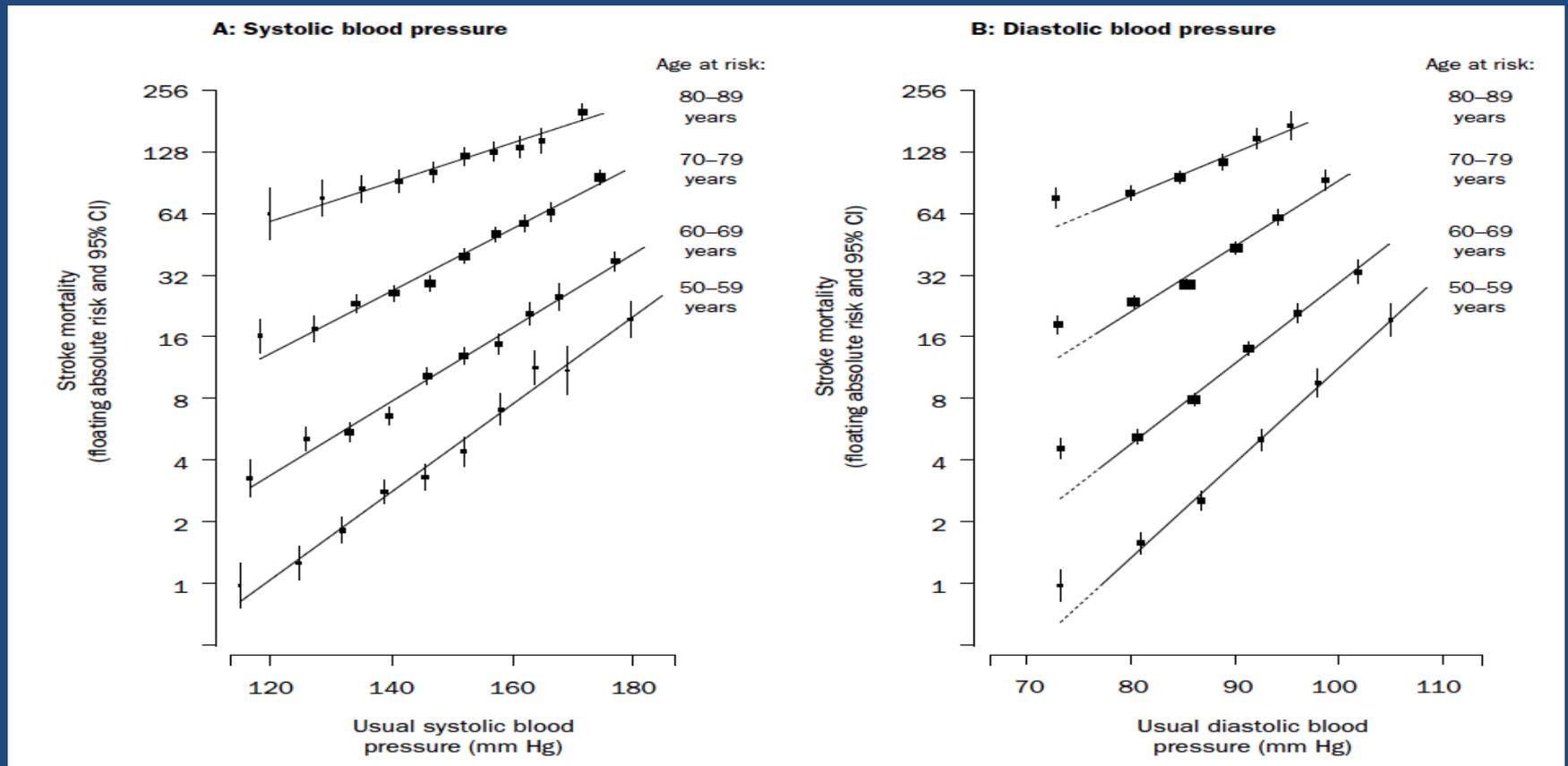


Dena Ettehad, Connor A Emdin, Amit Kiran, Simon G Anderson, Thomas Callender, Jonathan Emberson, John Chalmers, Anthony Rodgers, Kazem Rahimi

Lancet 2016; 387: 957-67



Stroke mortality rate in each decade of age versus usual BP at the start of that decade



Rates are plotted on a floating absolute scale, and each square has area inversely proportional to the effective variance of the log mortality rate. For diastolic BP, each age-specific regression line ignores the left-hand point (ie, at slightly less than 75 mm Hg), for which the risk lies significantly above the fitted regression line (as indicated by the broken line below 75 mmHg).

SPRINT Research Question

Examine effect of more intensive high blood pressure treatment than was recommended

↓
Randomized Controlled Trial
Target Systolic BP

↙
Intensive Treatment
Goal SBP < 120 mm Hg

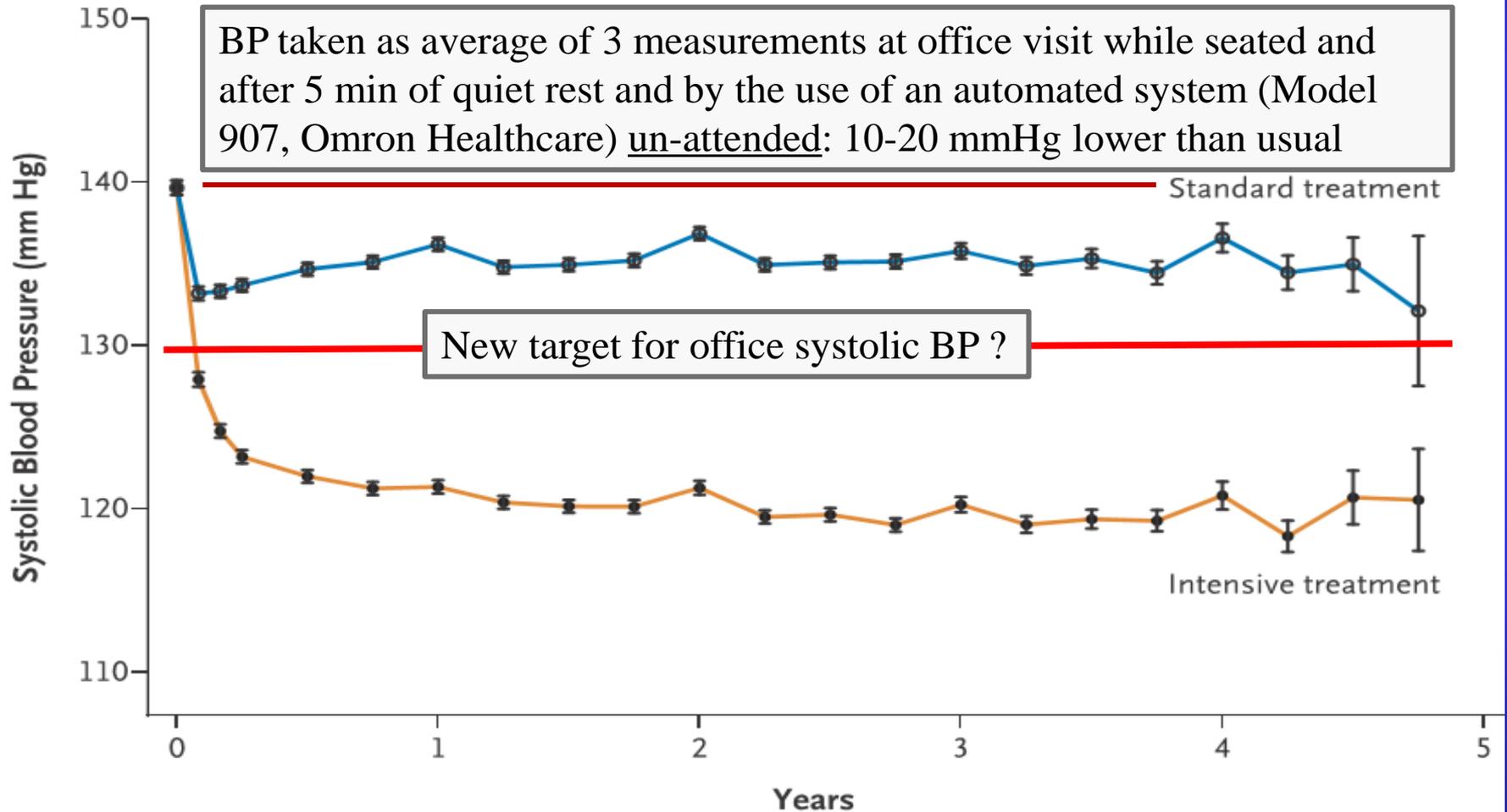
↘
Standard Treatment
Goal SBP < 140 mm Hg

SPRINT design details available at:

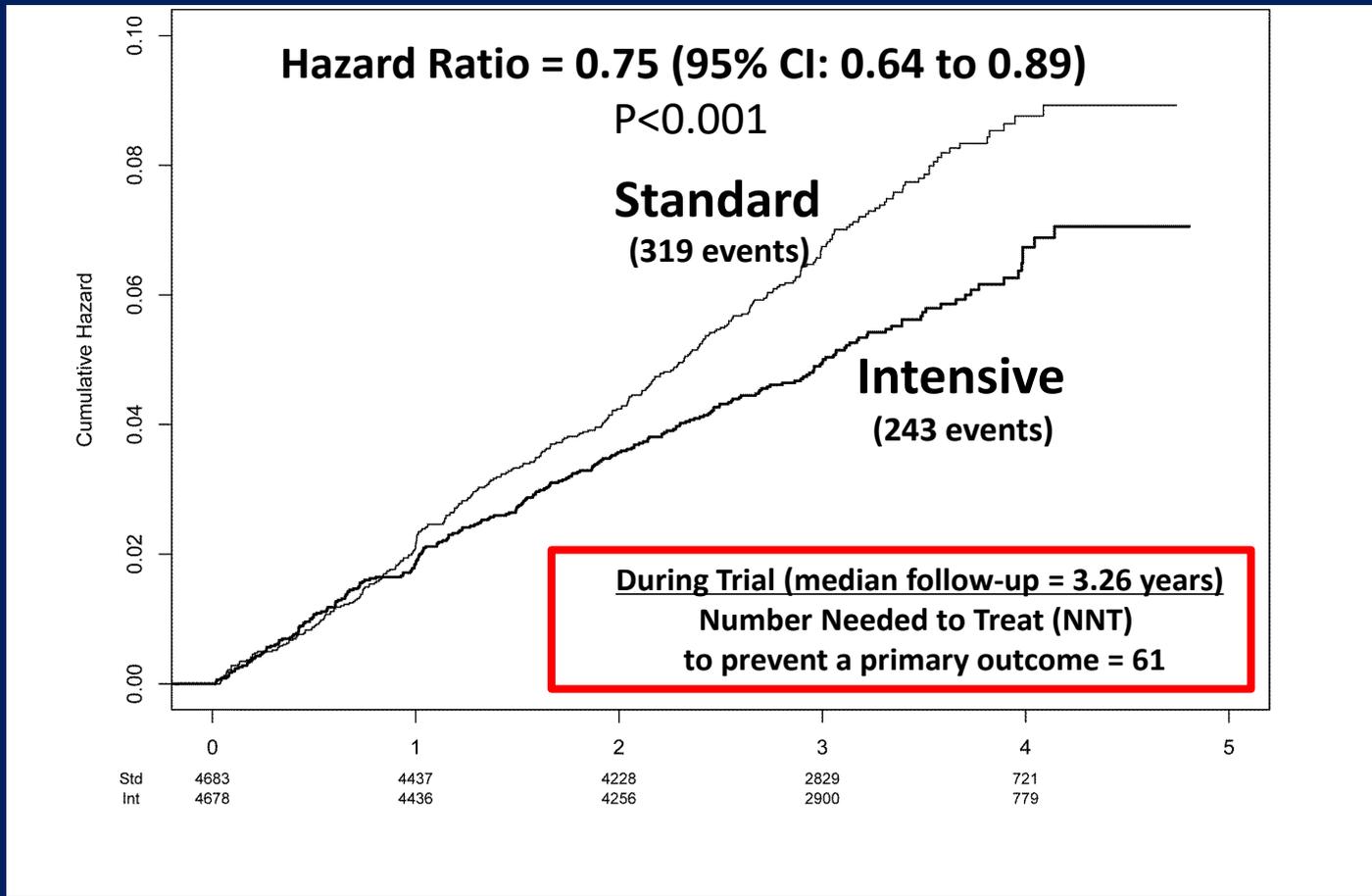
- [ClinicalTrials.gov \(NCT01206062\)](https://clinicaltrials.gov/ct2/show/study/NCT01206062)
- Ambrosius WT et al. Clin. Trials. 2014;11:532-546.

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*



SPRINT Primary Outcome Cumulative Hazard



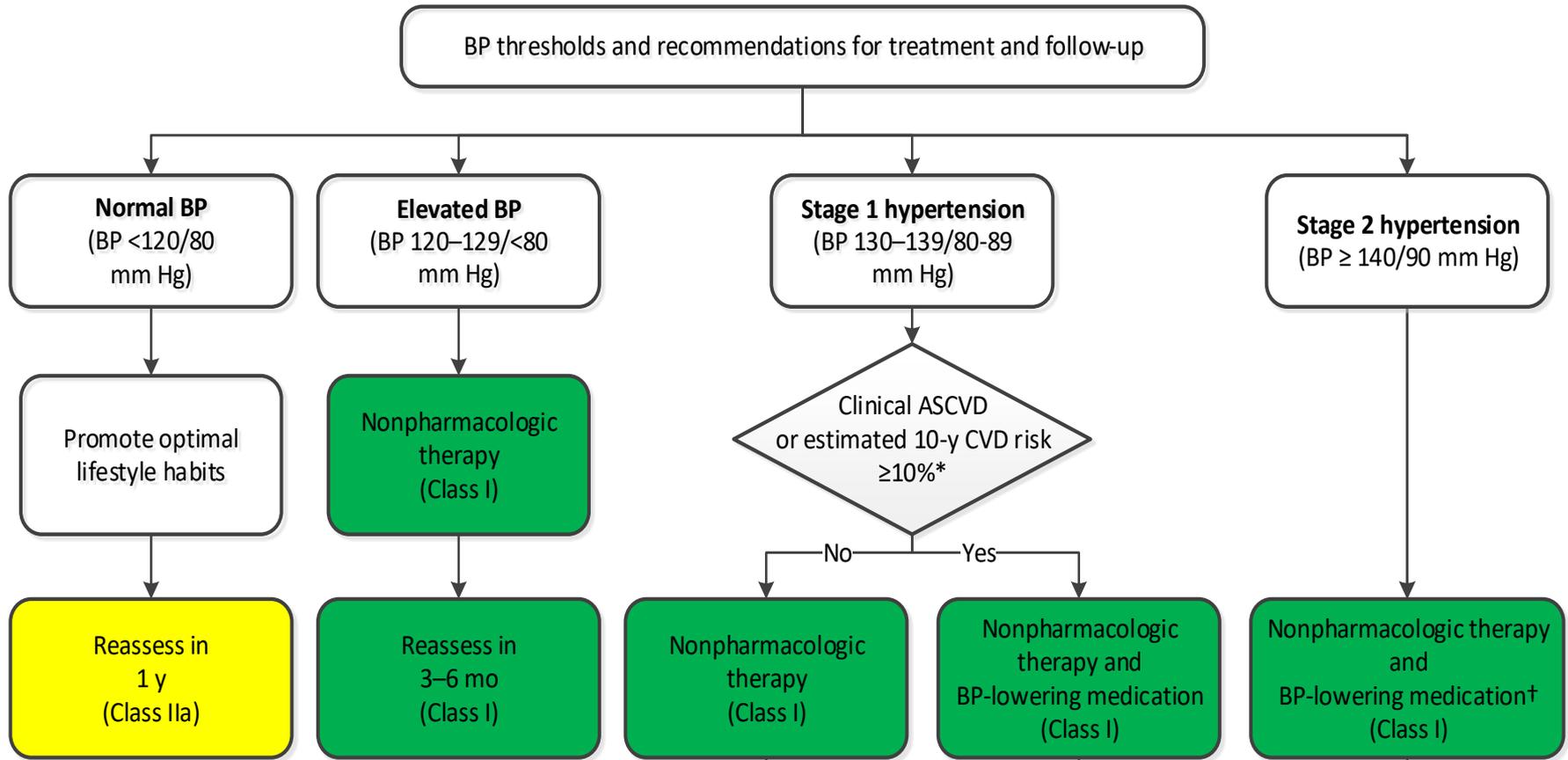
OPINION

Has the SPRINT trial introduced a new blood-pressure goal in hypertension?

Gema Ruiz-Hurtado, José R. Banegas, Pantelis A. Sarafidis, Massimo Volpe, Bryan Williams and Luis M. Ruilope

The SPRINT trial clearly shows that ‘lower is better’, providing justification for trying to lower blood-pressure targets.

Blood Pressure (BP) Thresholds and Recommendations for Treatment and Follow-Up





2018 ESC/ESH Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH)

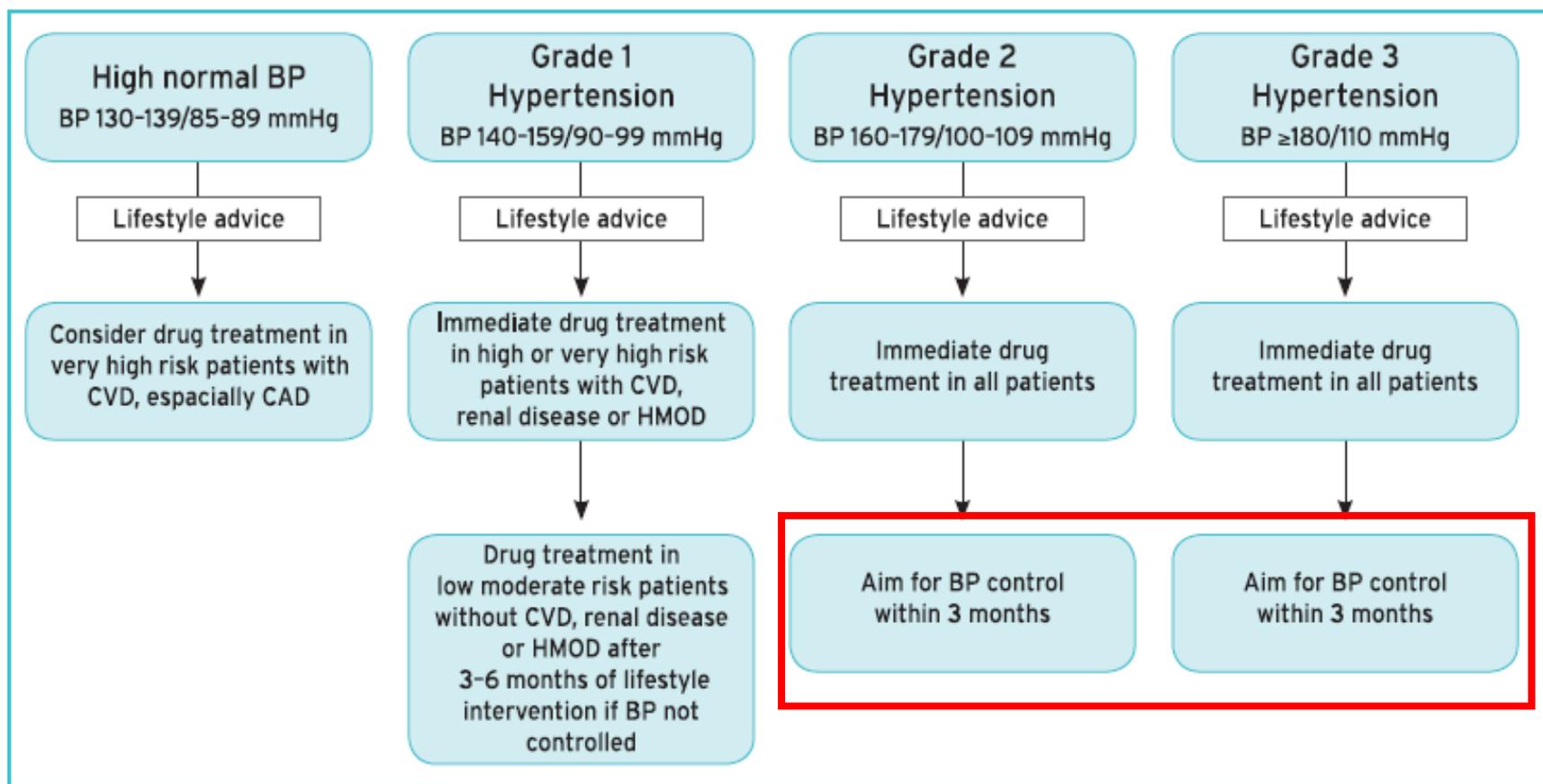
Authors/Task Force Members: Bryan Williams* (ESC Chairperson) (UK), Giuseppe Mancía* (ESH Chairperson) (Italy), Wilko Spiering (The Netherlands), Enrico Agabiti Rosei (Italy), Michel Azizi (France), Michel Burnier (Switzerland), Denis L. Clement (Belgium), Antonio Coca (Spain), Giovanni de Simone (Italy), Anna Dominiczak (UK), Thomas Kahan (Sweden), Felix Mahfoud (Germany), Josep Redon (Spain), Luis Ruilope (Spain), Alberto Zanchetti[†] (Italy), Mary Kerins (Ireland), Sverre E. Kjeldsen (Norway), Reinhold Kreutz (Germany), Stephane Laurent (France), Gregory Y. H. Lip (UK), Richard McManus (UK), Krzysztof Narkiewicz (Poland), Frank Ruschitzka (Switzerland), Roland E. Schmieder (Germany), Evgeny Shlyakhto (Russia), Costas Tsioufis (Greece), Victor Aboyans (France), and Ileana Desormais (France)

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Office blood pressure treatment target range according to 2018 ESC/ESH Guidelines

| Age group | Office SBP treatment target ranges (mmHg) | | | | | Office DBP treatment target range (mmHg) |
|---|--|--|--|--|--|--|
| | Hypertension | + Diabetes | + CKD | + CAD | + Stroke ^a /TIA | |
| 18 - 65 years | Target to 130 <i>or lower if tolerated</i> Not <120 | Target to 130 <i>or lower if tolerated</i> Not <120 | Target to <140 to 130 <i>if tolerated</i> | Target to 130 <i>or lower if tolerated</i> Not <120 | Target to 130 <i>or lower if tolerated</i> Not <120 | 70–79 |
| 65 - 79 years ^b | Target to 130-139 <i>if tolerated</i> | Target to 130-139 <i>if tolerated</i> | Target to 130-139 <i>if tolerated</i> | Target to 130-139 <i>if tolerated</i> | Target to 130-139 <i>if tolerated</i> | 70–79 |
| ≥80 years ^b | Target to 130-139 <i>if tolerated</i> | Target to 130-139 <i>if tolerated</i> | Target to 130-139 <i>if tolerated</i> | Target to 130-139 <i>if tolerated</i> | Target to 130-139 <i>if tolerated</i> | 70–79 |
| Office DBP treatment target range (mmHg) | 70–79 | 70–79 | 70–79 | 70–79 | 70–79 | |

Initiation of blood pressure-lowering treatment of hypertension according to 2018 ESC/ESH Guidelines



2018 ESC/ESH Guidelines

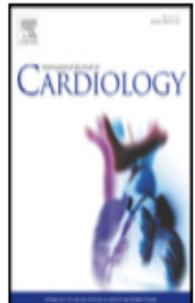
Goal in 3 months!



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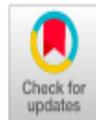


Is early and fast blood pressure control important in hypertension management?

Massimo Volpe^{a,b,*}, Giovanna Gallo^a, Giuliano Tocci^{a,b}

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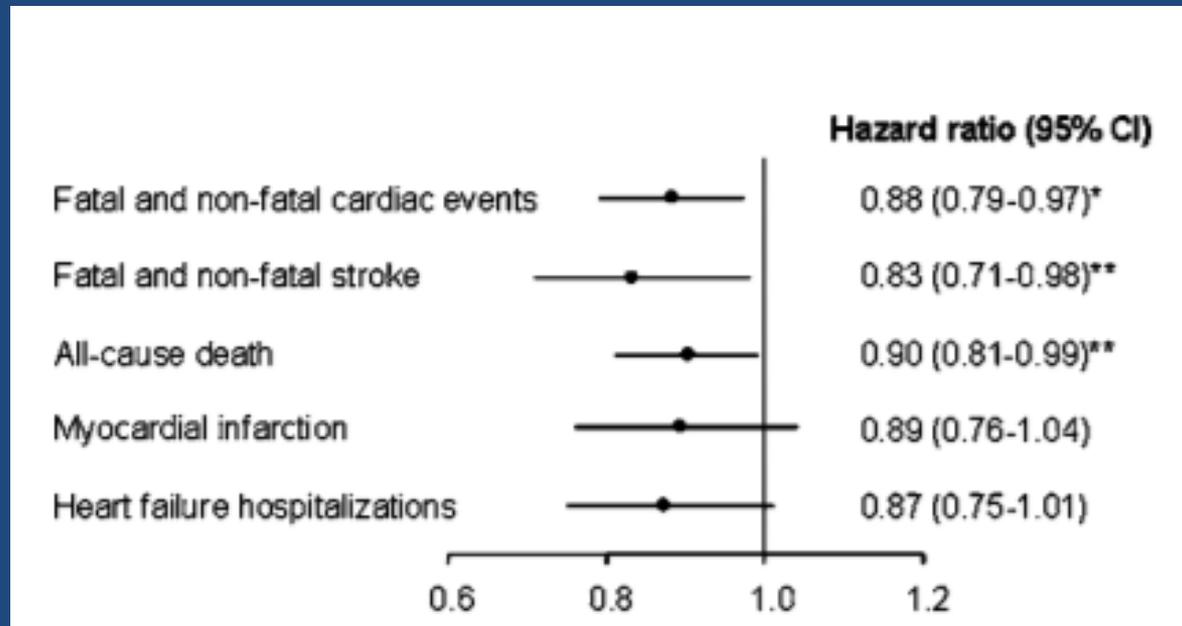
^b IRCCS Neuromed, Pozzilli, IS, Italy



REVIEW

How early should blood pressure control be achieved for optimal cardiovascular outcomes?

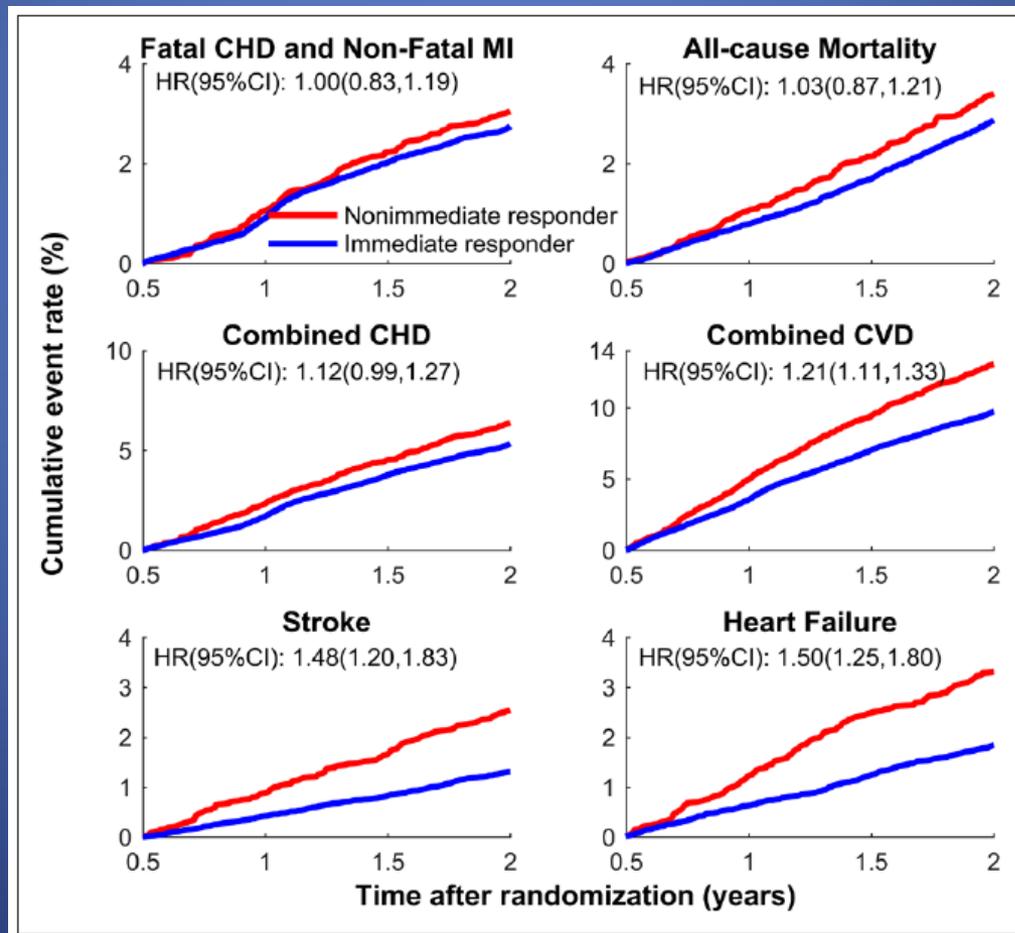
MR Weir¹, D Zappe², LA Orloski³ and JR Sowers⁴



Prompt BP control—within 6 months but ideally within 1 to 3 months—appears to confer improved outcomes in hypertensive patients, particularly those with stage 2 hypertension and/or at high CV risk.

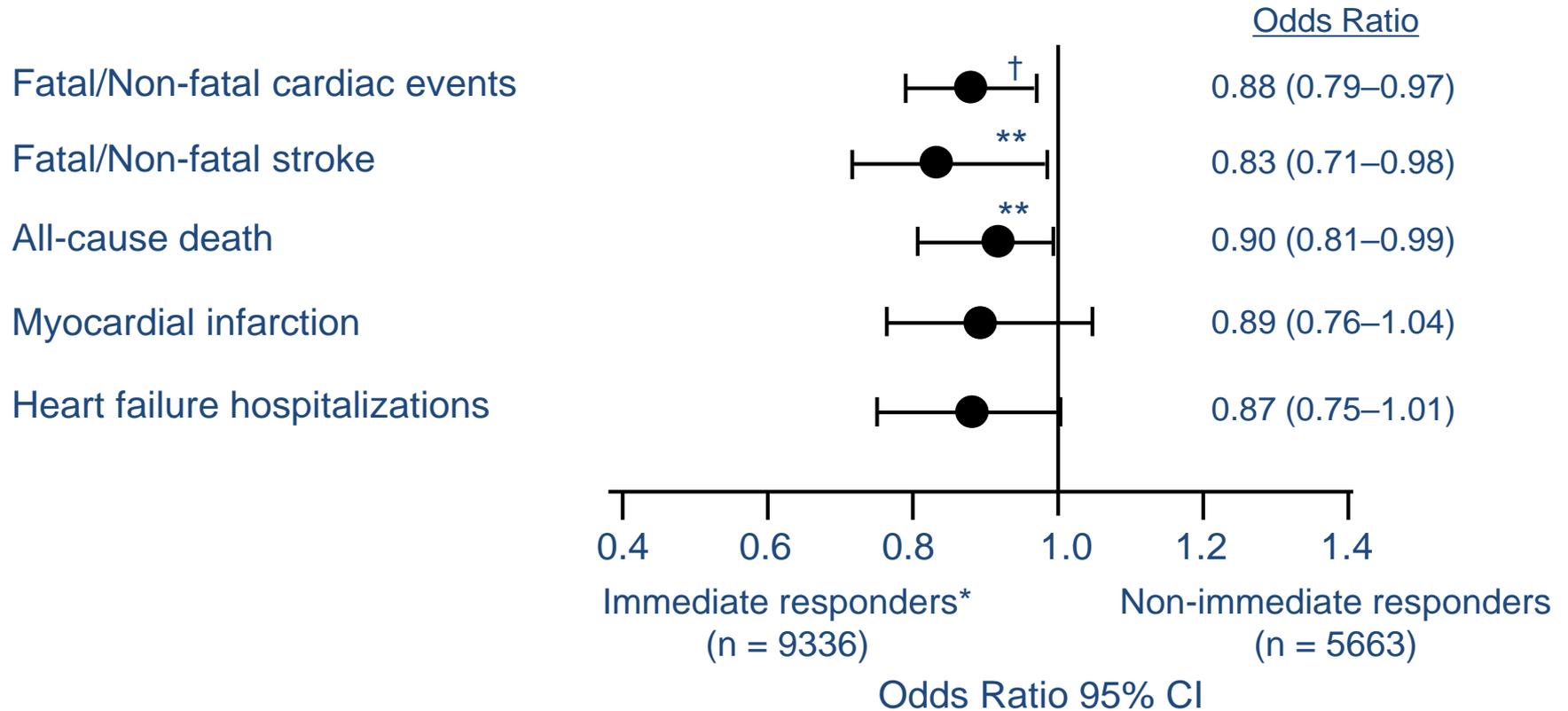
Clinical Trials

Heterogeneity in Early Responses in ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial)



VALUE: Analysis of Results Based on Immediate Response*

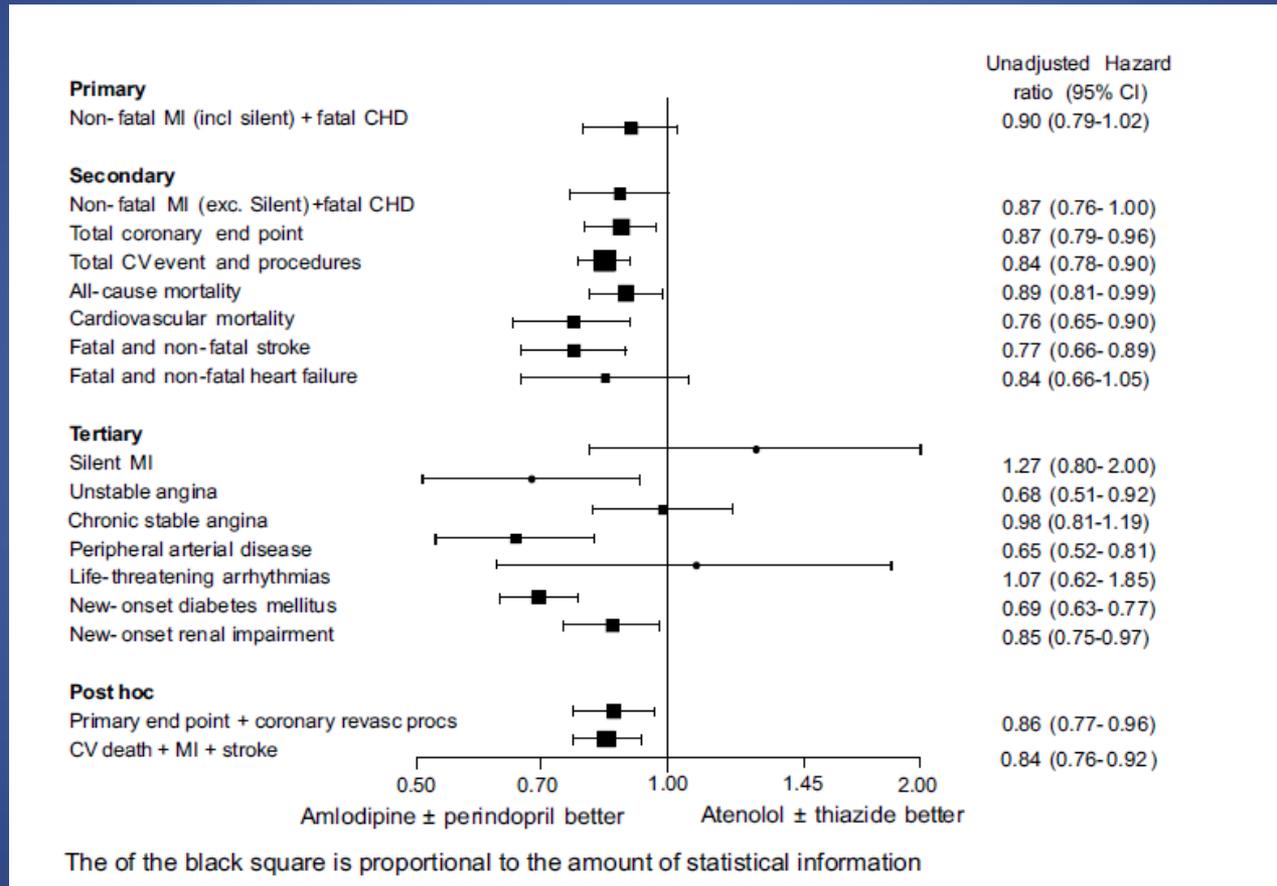
Pooled Treatment Groups



*Those not on previous tx: SBP ↓ ≥10 mmHg at one month;
those on previous tx: no increase in SBP when switched to study drug

** $P < 0.05$; † $P < 0.01$.

Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial



The superiority of amlodipine-based vs. atenolol-based therapy, in reducing fatal and non-fatal stroke, total CV events and procedures and all-cause mortality, has been attributed to the early BP lowering effect of amlodipine during the first year of treatment

Why are BP control rates still poor?

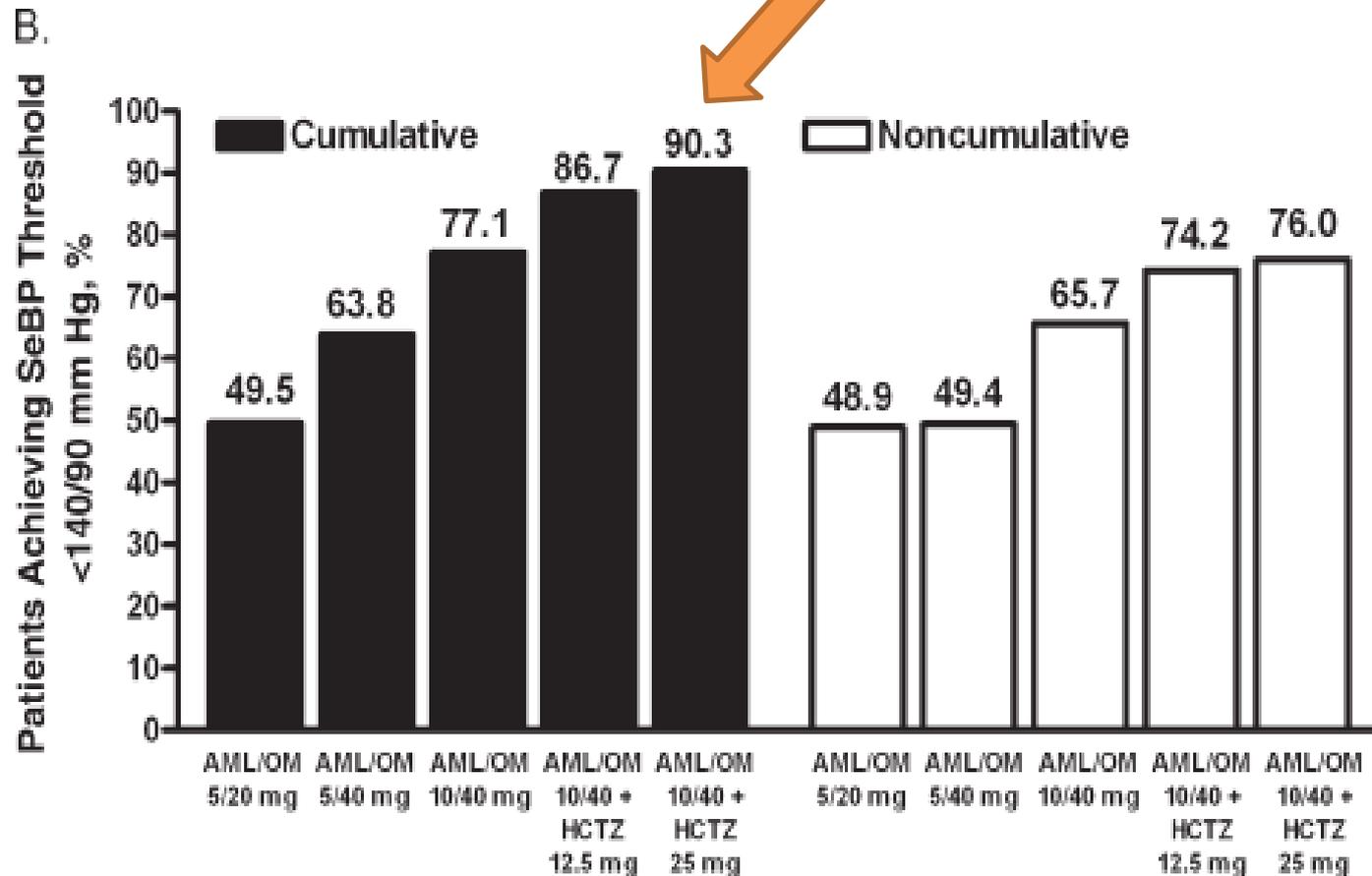
- The drugs don't work?
- The patients don't take them ?
- Treatment guidelines are too complex?

- ...And how will we manage to achieve lower BP targets?

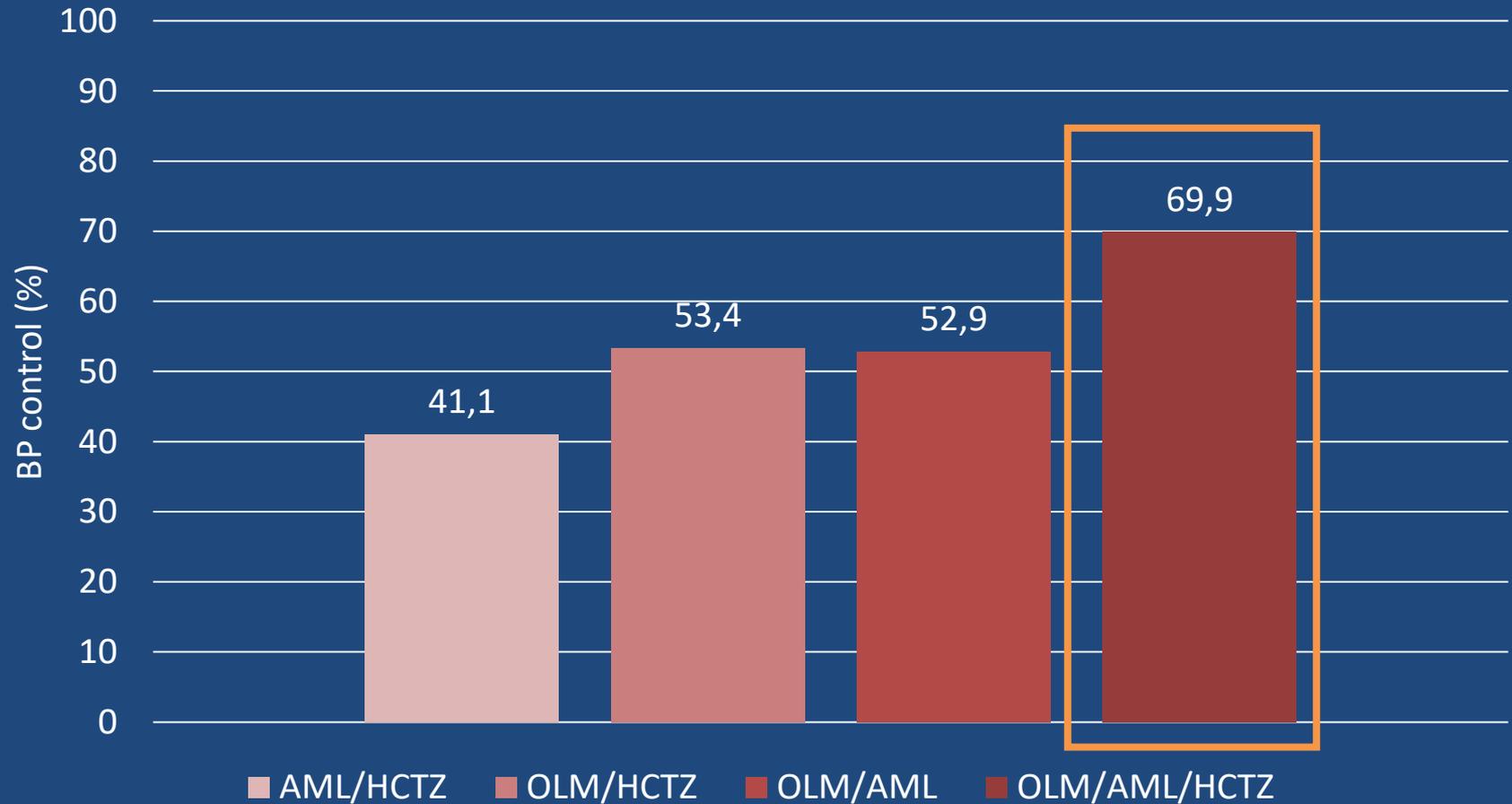
Rationale for combination therapy in hypertension treatment: Better CV outcomes and improved event-free survival

- Vast majority of hypertensive patients with different CV risk profiles included in large, randomised clinical trials have been treated with combination therapy (not monotherapy).
- Combination therapy was initiated early during each trial and maintained throughout the follow-up, to ensure effective and sustained BP control.
- Combination therapy predominantly included CCB-based strategies combined with either ACE inhibitors or ARBs.

Proportions of patients achieving Seated Blood Pressure (SeBP) threshold of <140 / 90 mmHg by titration dose with different combination therapies based on olmesartan/amlodipine/HCTZ



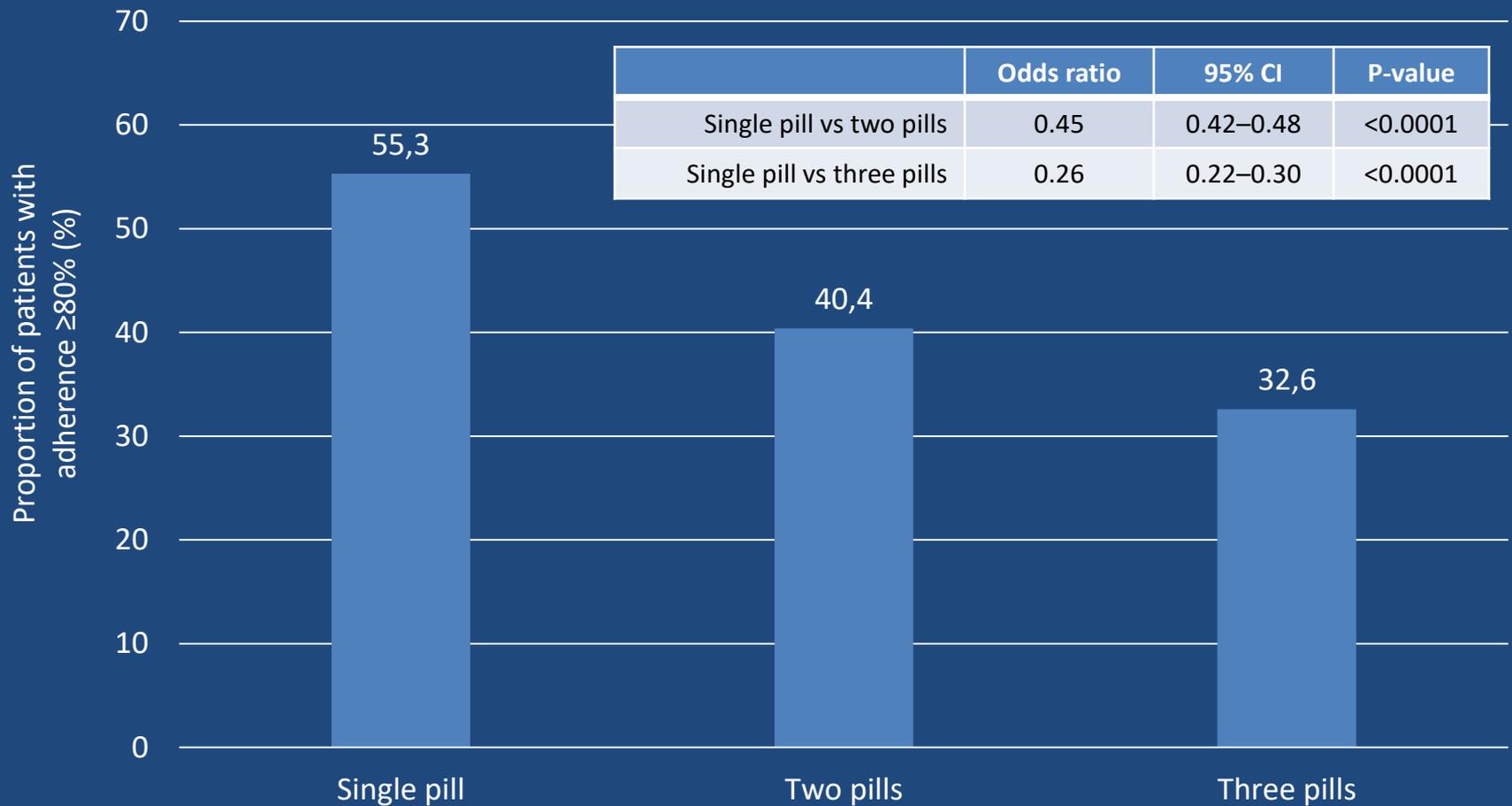
Better BP goal[†] achievement with triple combination therapy (OLM/AML/HCTZ)



*p<0.001 vs. dual combination

[†]BP goal defined as <140/90 mmHg

Single-pill fixed-dose combinations are associated with greater adherence in hypertension

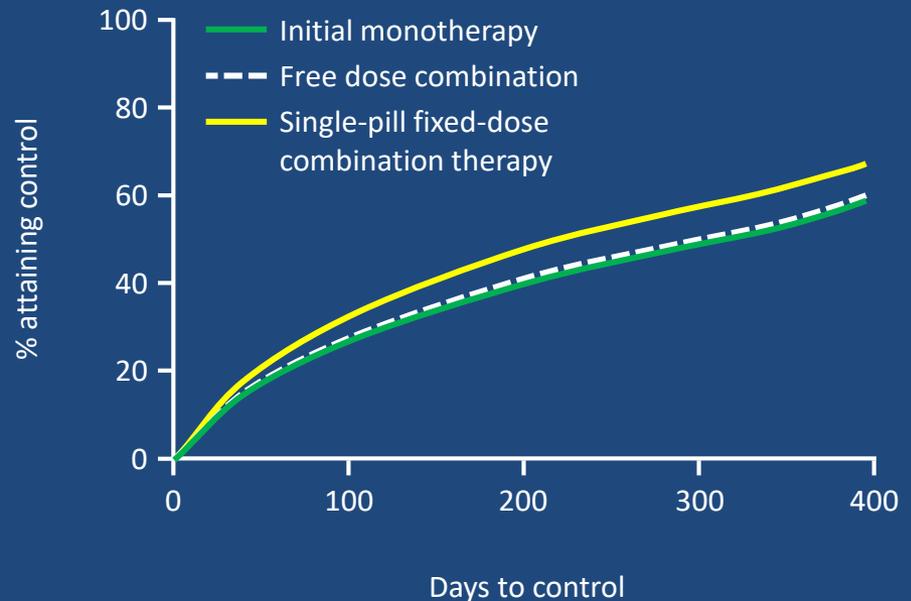


After 12 months, patients given initial combination therapy had a greater chance of BP control than initial monotherapy, and this was even greater for single-pill fixed-dose combination therapy

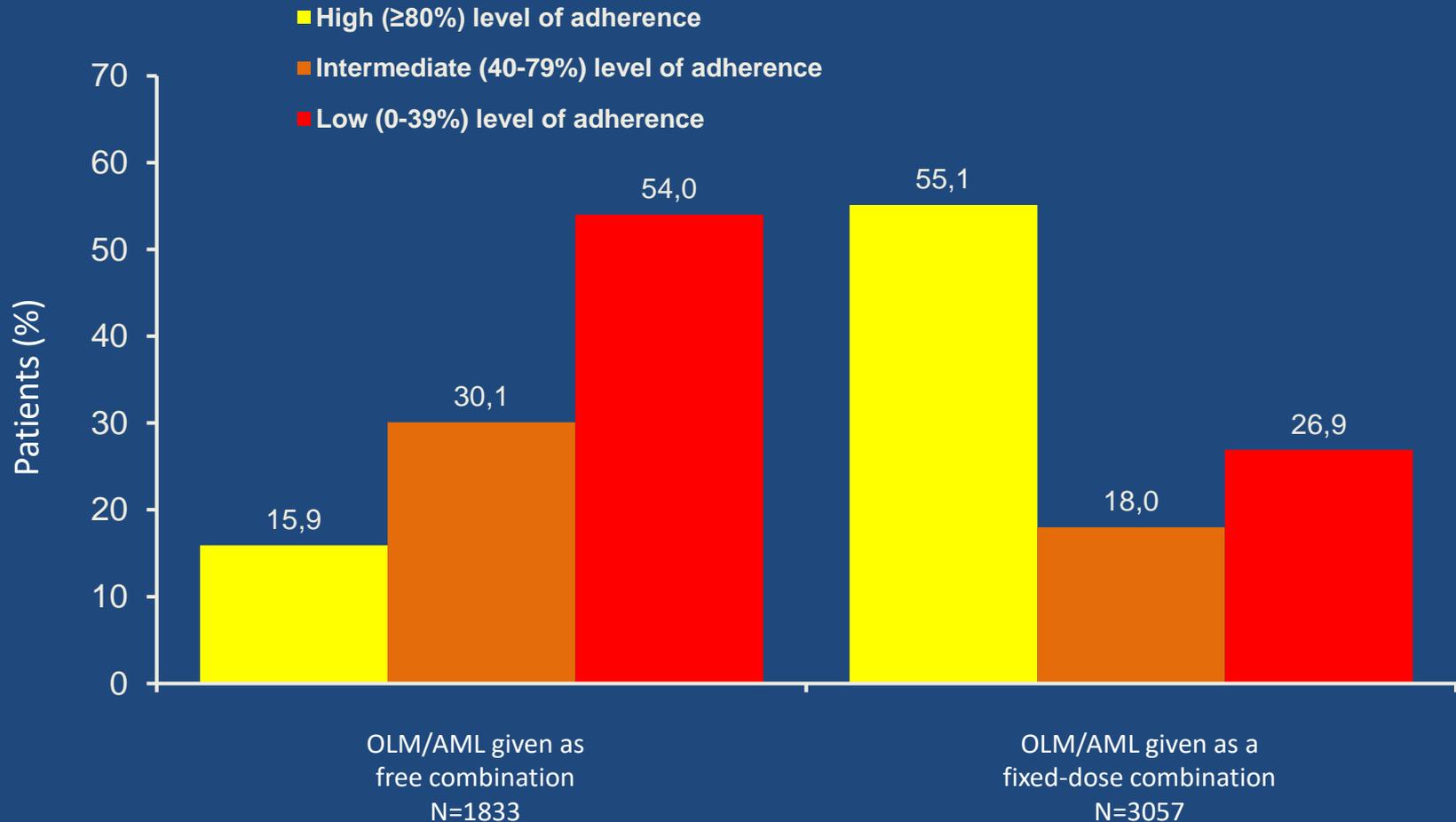
Retrospective analysis of electronic record data from 180 US clinics (n=106,621)

Compared with monotherapy (reference):

- Initial therapy with single-pill combinations was associated with a 53% greater chance of achieving BP in the first year (HR, 1.53 [95% CI, 1.47–1.58])
- Initial therapy with free dose combinations was associated with a 34% greater chance of BP control (HR, 1.34; [95% CI, 1.31–1.37])



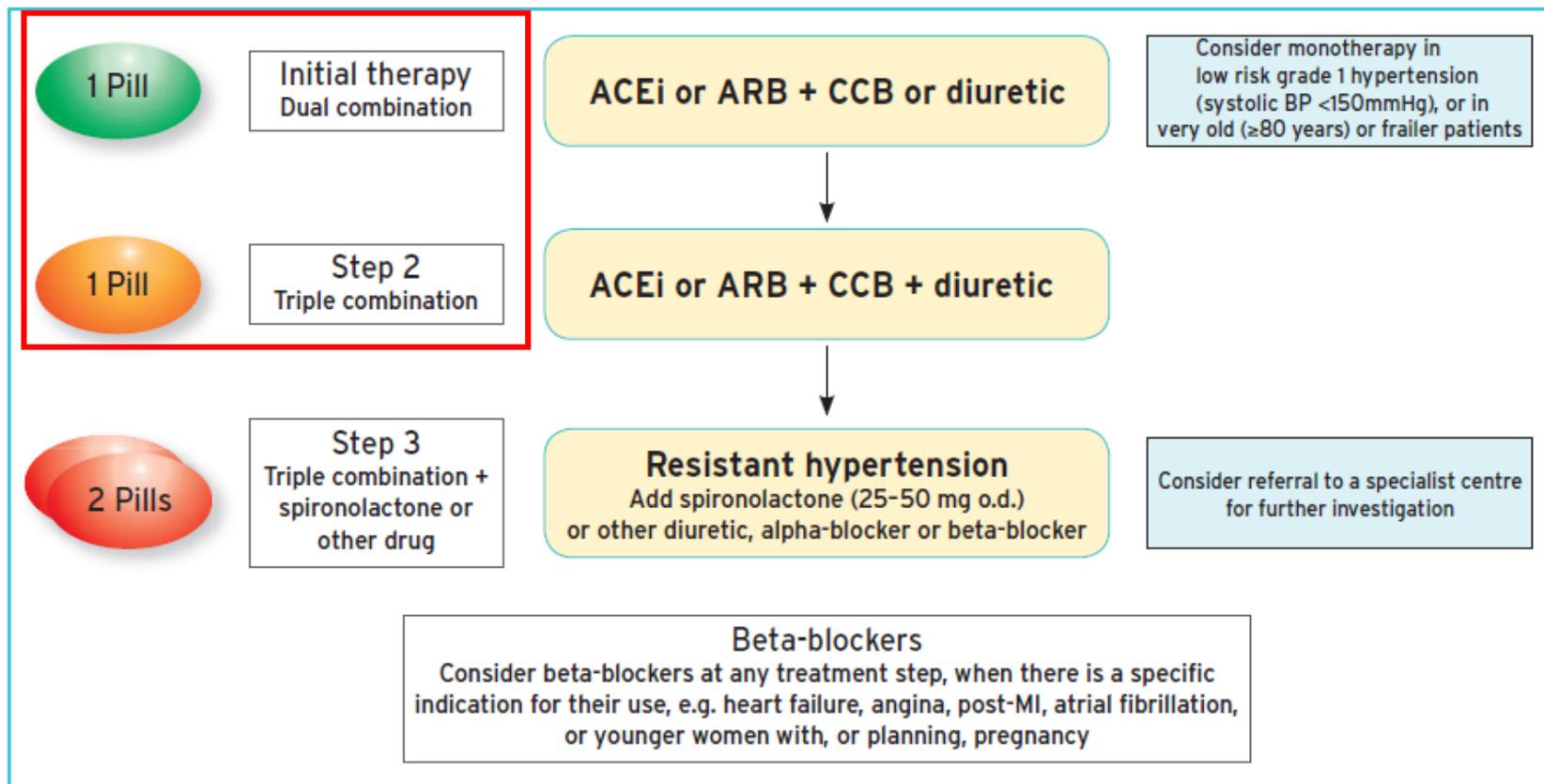
A Single Pill Combination was superior to a free combination of the same drugs in an Italian general practice database



Single-pill combination

- Poor adherence to longer-term BP-lowering medication is now recognized as a major factor contributing to poor BP control rates.
- Research has shown a direct correlation between the number of BP-lowering pills and poor adherence to medications.
- Moreover, SPC therapy has been shown to improve adherence to treatment.
- **SPC therapy is now the preferred strategy for initial two-drug combination treatment of hypertension and for three-drug combination therapy when required.**
- This will control the BP of most patients with a single pill and could transform BP control rates.

Treatment strategy for uncomplicated hypertension



Summary and Conclusions

- BP control is still suboptimal, although significant improvements have been achieved worldwide and also in Europe.
- Combination therapy has been widely used in clinical trials and is reported to achieve BP control in up to 90% of patients.
- The use of single-pill combination approach is an essential tool to face the low adherence problem.
- Practical tools, such as a therapeutic platform for the use of combination therapy, may support physicians' management of hypertension and ensure higher adherence and better BP control.

What's next?

- Our generation of physicians has a concrete chance to control about 100% of hypertensive patients and to lead towards a major reduction in cardiovascular disease burden.
- International collaborations and networks, aiming at this goal also through a novel approach to practical recommendations, are required to achieve this ambitious healthcare target.

Thank You for Your Attention!

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