INITIAL COMBINATION THERAPY IN HYPERTENSION

THS. BS. NGUYỄN NGỌC THANH VÂN

ĐẠI HỌC Y DƯỢC TPHCM

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Combination therapy at the start of hypertension treatment: pros and cons

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Dr. Ngoc-Thanh-Van Nguyen

The universal agreement on initiating two-drug therapy in hypertensives with blood pressure ≥140/90 mmHg has not been sufficiently translated into real-world practice, leading to treatment failure. Evidence supporting this ESC guideline recommendation includes more rapid, sustained control due to the antihypertensive and non-antihypertensive effect, an acceptable safety profile, and a more homologous response. A single-pill combination promotes less therapeutic inertia, more patient adherence and monetary savings. Concerns remain in the elderly, frail individuals, pseudo-resistance, consequences of dose confusion, polypharmacy and high pill burden. While the net clinical benefit favours an initial two-drug therapy, physicians should be vigilant in relation to vulnerable patients and individualise therapy accordingly.

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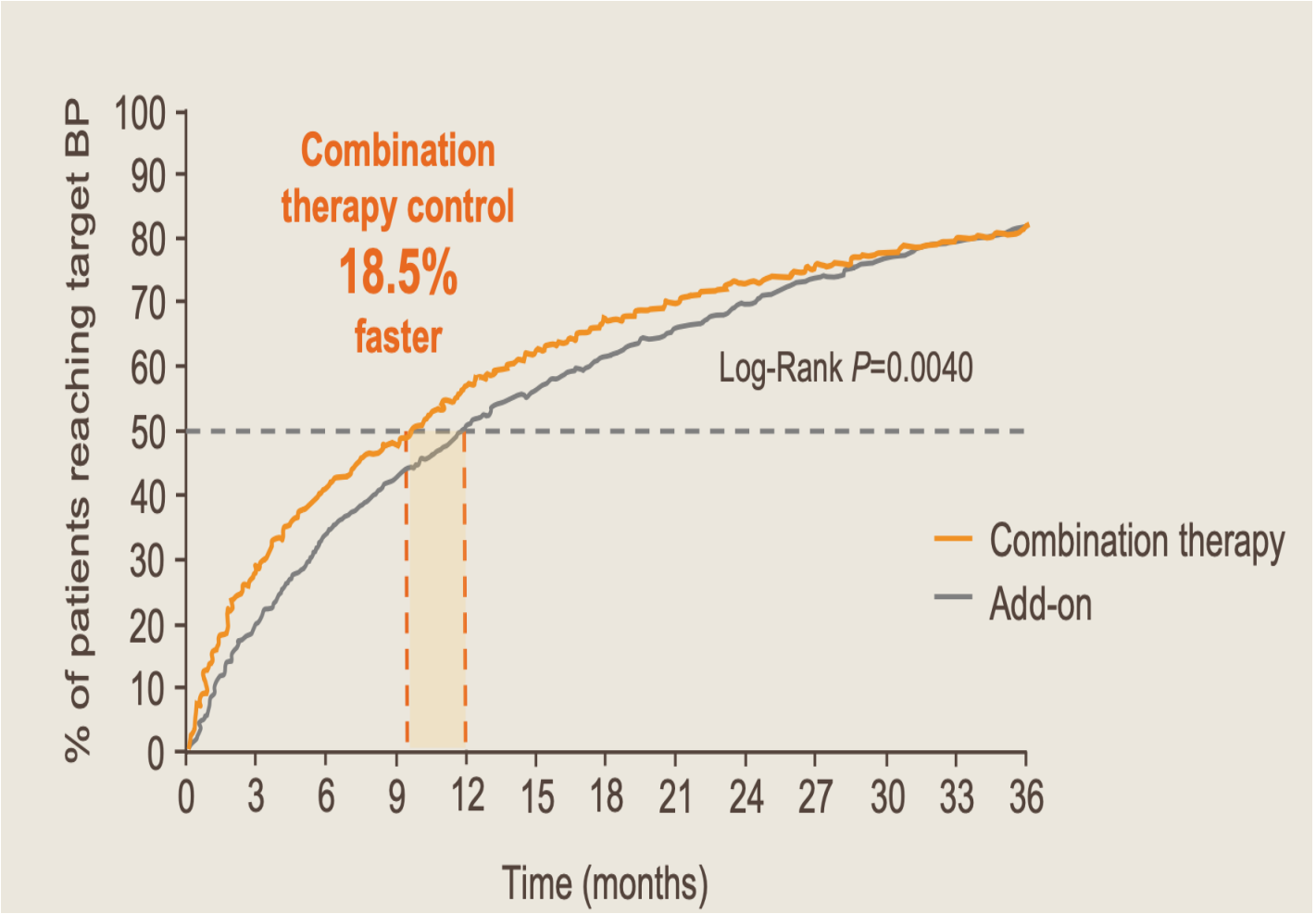
01

TIME

TIME TO CONTROL

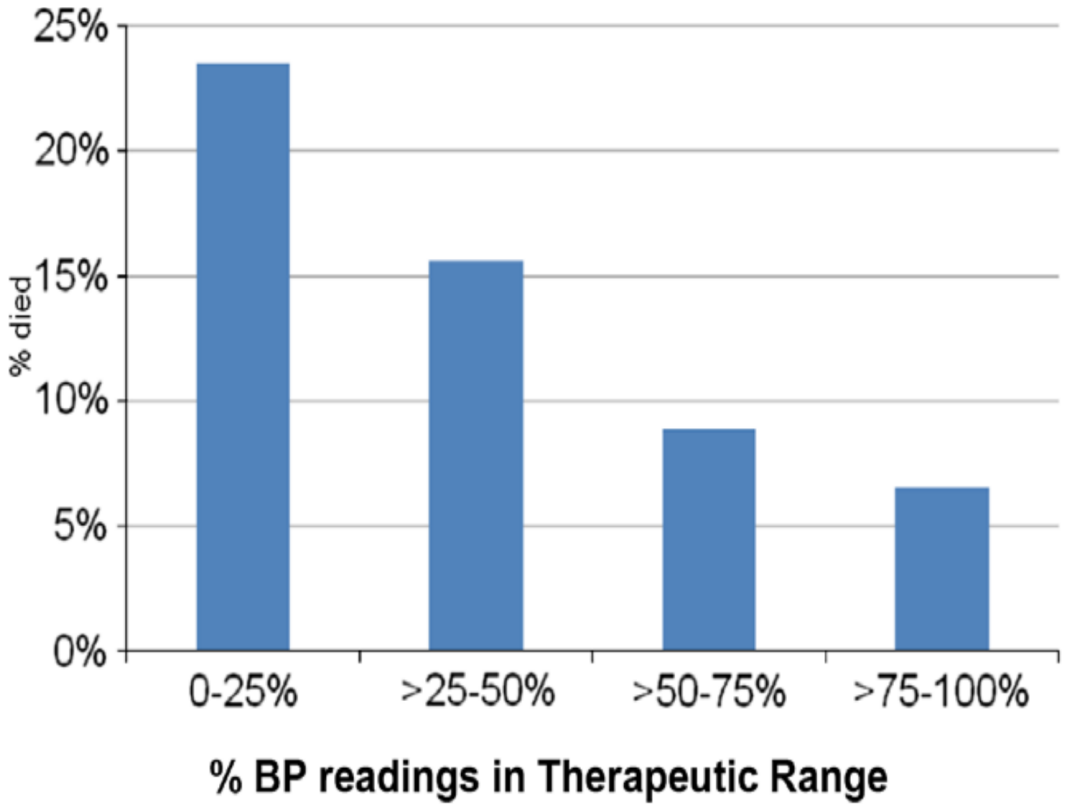
"23% risk reduction

for CV events or death"



Gradman AH. Hypertension 2013

IME IN CONTROL

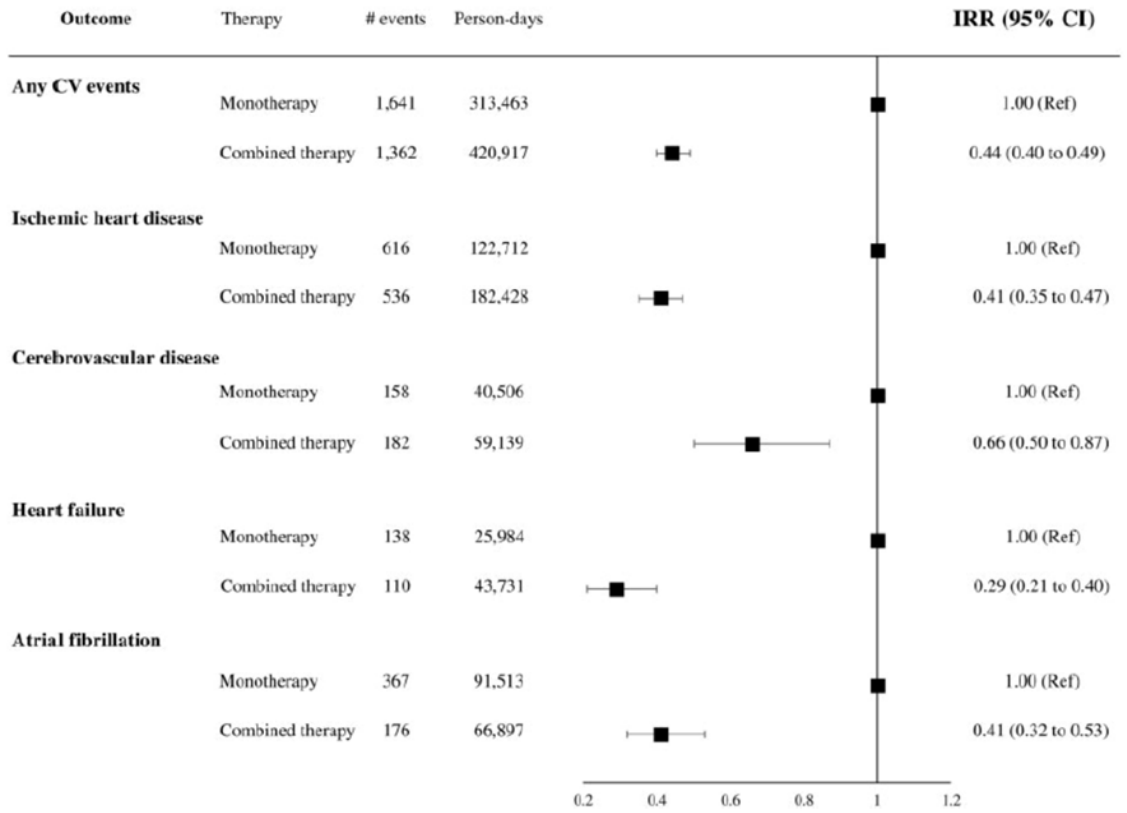


Time at TaRgEt - TITRE

TITRE Outcome	Difference in Hazard Ratio Zero time in BP control versus 9-12 months in BP control (<140/90mmHg)
CV Death or MI or Stroke	74% reduction
All cause Death	47% reduction

https://doi.org/10.1371/journal.pone.0202359
https://doi.org/10.1161/JAHA.117.007131

Early Cardiovascular Protection by initial two-drug single pill combination versus monotherapy in hypertension



N = 37,078 monotherapy
N = 7,456 SPC
2,212 CV events at 1 year

The effect of starting treatment with a SPC versus Monotherapy on 1 year risk of CV outcomes

Outcome	HR[a] (95% CI)	*P*-value
Any CV event	0.85 (0.74–0.97)	0.02
Ischaemic heart disease	0.73 (0.56–0.95)	0.02
Cerebrovascular disease	0.83 (0.61–1.14)	0.26
Heart failure	0.90 (0.54–1.51)	0.69
Atrial fibrillation	0.63 (0.42–0.94)	0.02

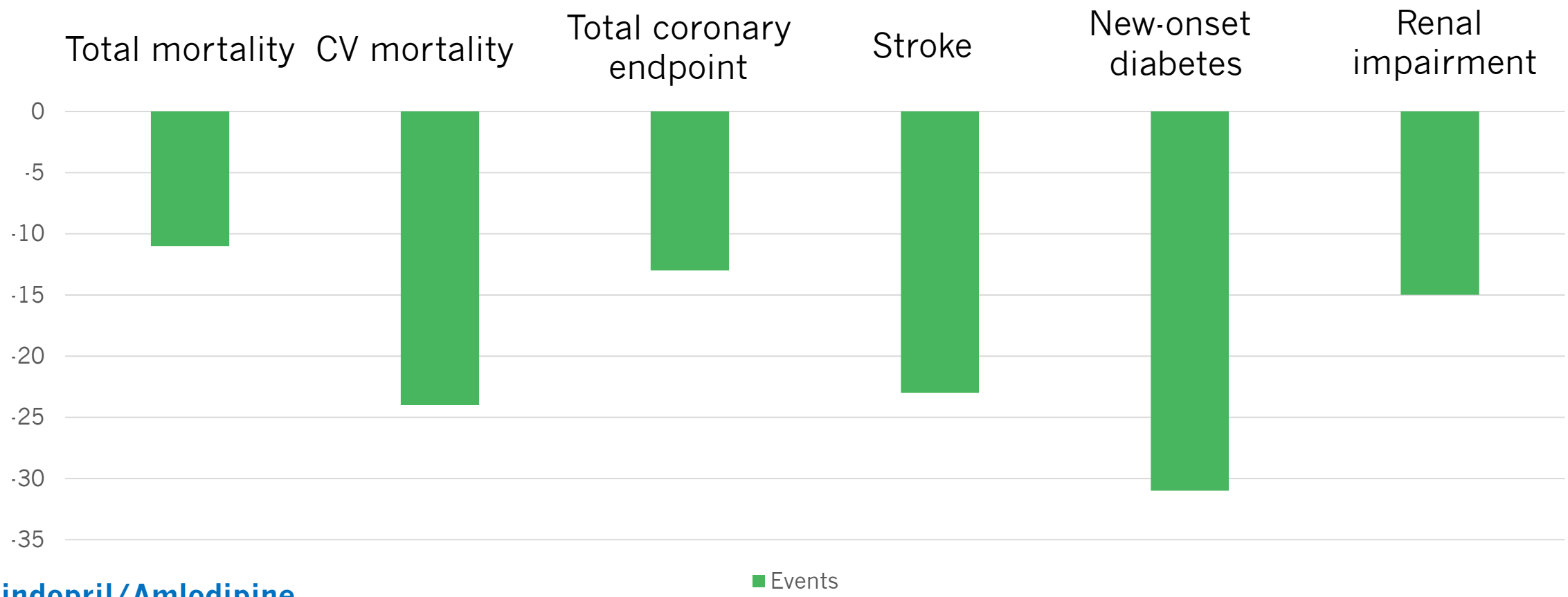
High dimensional propensity score matched in 2212 patients with events at 1 year

Rea F, et al. Eur Heart J, 2018

Healthcare utilization Database | Lombardi, Italy

NON-ANTIHYPERTENSIVE EFFECTS

Atenolol/Bendroflumethiazide



Perindopril/Amlodipine

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ASCOT BPLA Study Lancet 2005

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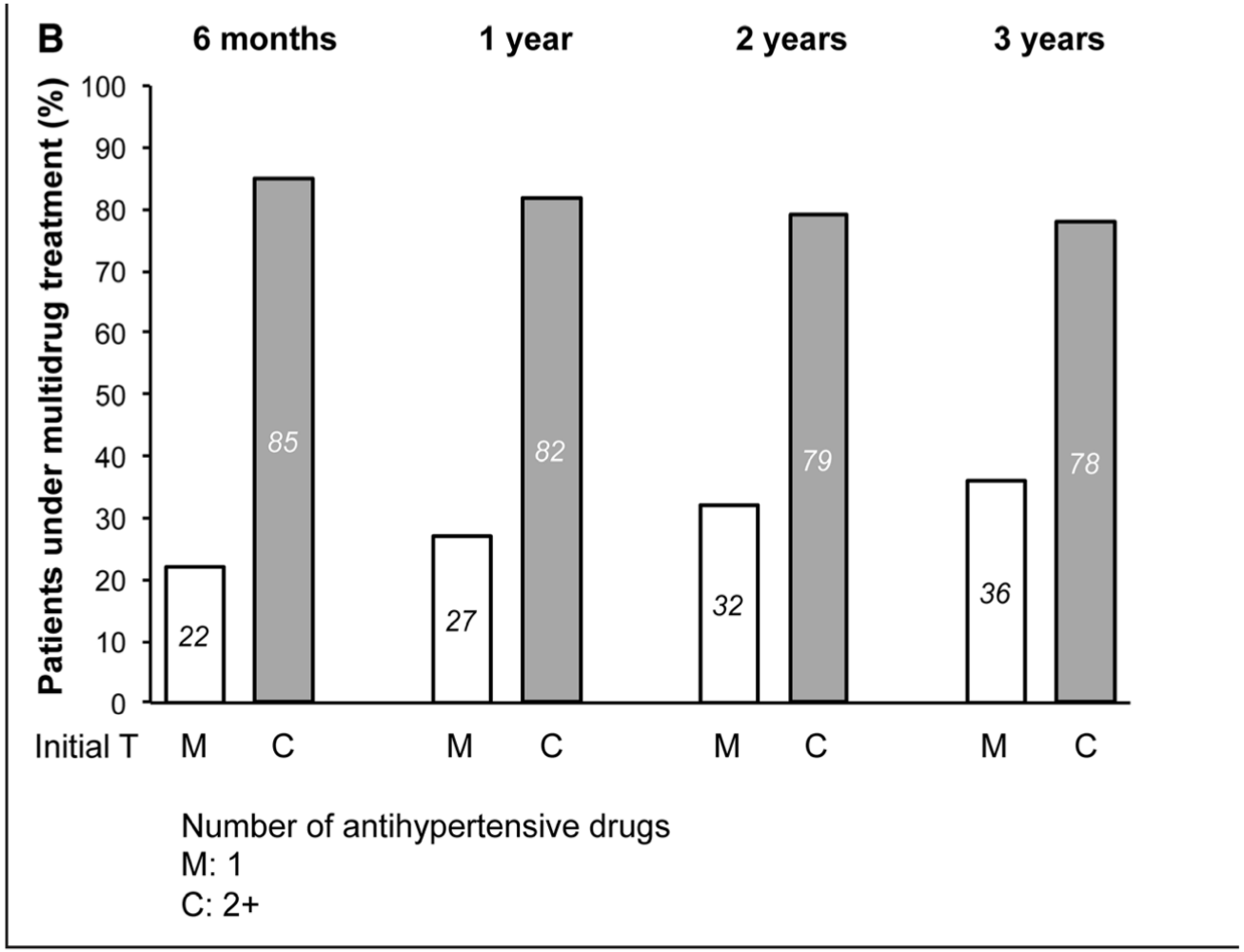
REALWORLD PRACTICE

"Most start with Monotherapy

...Will likely stay with Monotherapy"



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Rea F, et al. Hypertension 2018

SPRINT IN NUMBERS

167 NNT to prevent 1 CV death

83 NNT to prevent all-cause death

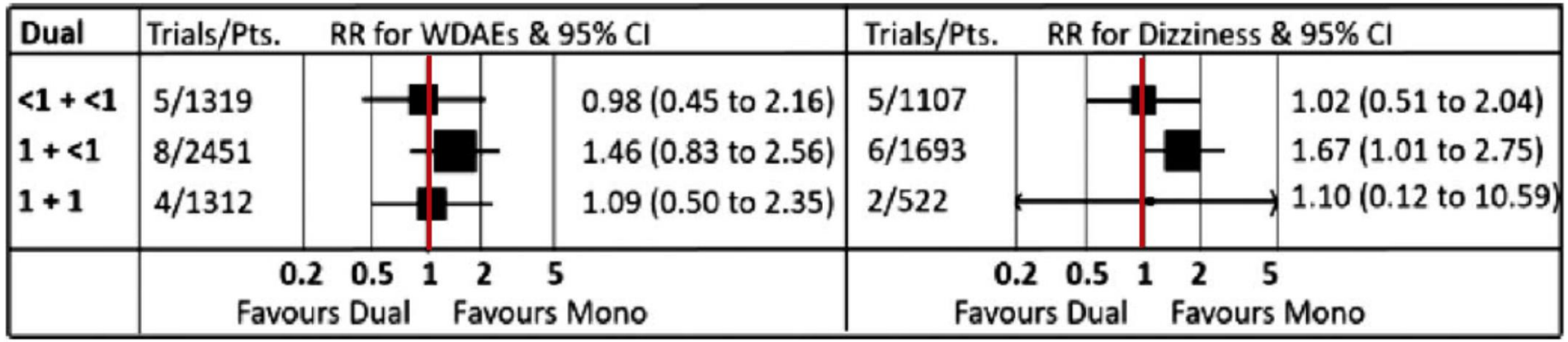
56 NNH to cause 1 case of AKI or renal failure

42 NNH to cause 1 SAE

Efficacy and Safety of Dual Combination Therapy as Initial Treatment for Hypertension - A Systematic Review and Meta-Analysis

33 trials, 13,095 participants, mean baseline mean BP 155/100mmHg
Compared low-top standard dose dual combinations <1 + <1, 1 + <1, 1+1

Withdrawals for Adverse Events (WDAE) - Dual vs. Mono therapy



Conclusion: *Compared with standard-dose monotherapy, initiating treatment with low-standard-dose dual combination therapy is more efficacious without increasing withdrawals for adverse events…..these data support the ESC-ESH and US Hypertension guideline recommendations…..*

Salam A, et al. J Hypertens 2019

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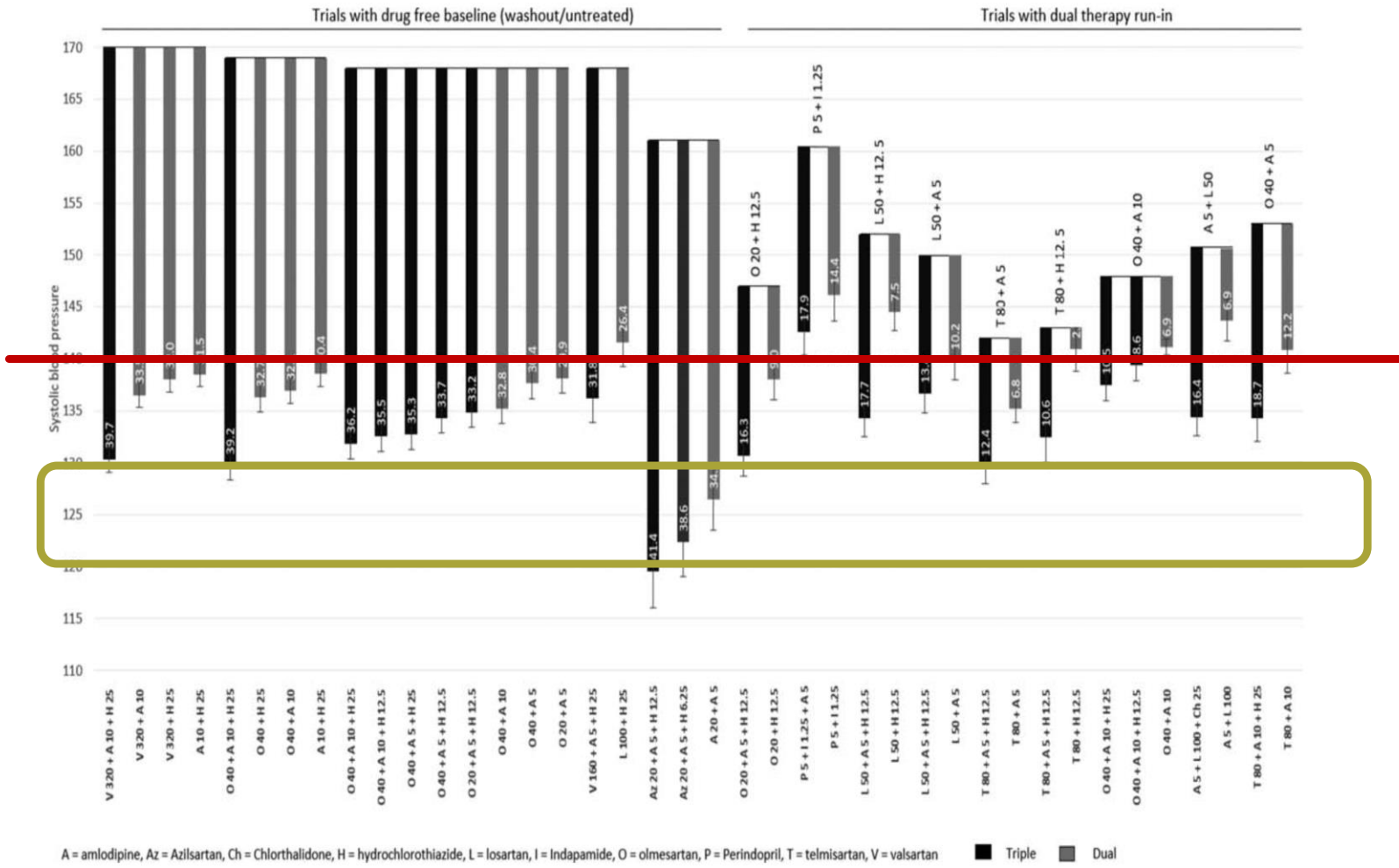
TRIPPLE THERAPY

"45% - 58%"

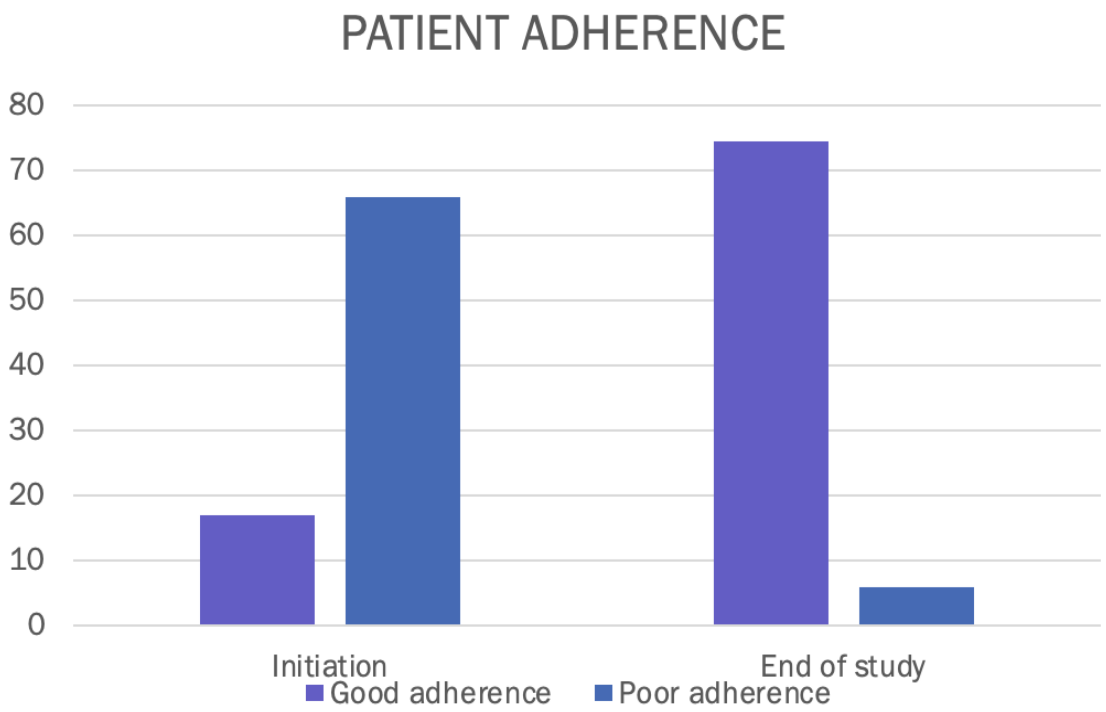


NGOC THANH VAN NGUYEN, MD- NTCC 2019, HCMC

Salam A, Journal of Hypertension.2019

IMPROVED ADHERENCE IN TRIPPLE THERAPY

Perindopril/Indapamide/Amlodipine

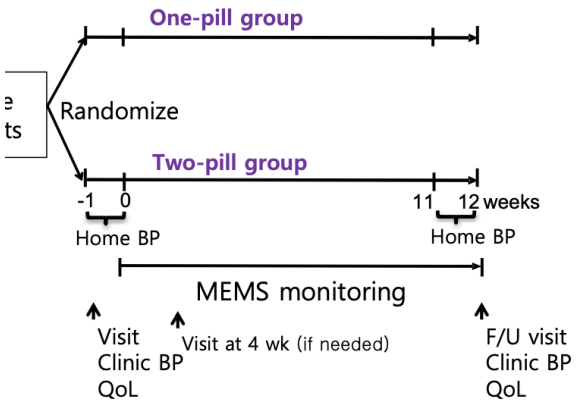


- 1.1% Discontinuation
- 0.58% due to AEs
- 0.8 % nonWAEs

Kobalava et al, Kardiologiia 2018
Kostas T et al, Clin Drug Invest 2019

Study design

Multi-center, open-label, parallel group randomized controlled trial



One-pill group:

Triple-component SPC: Olmesartan + Amlodipine + HCTH, 5/20/12/5 mg

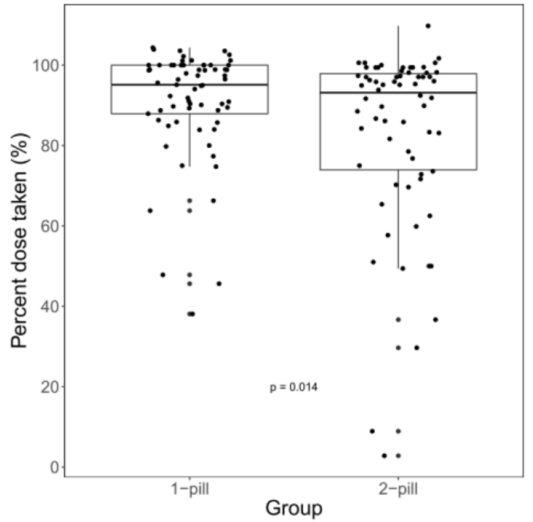
Two-pill group:

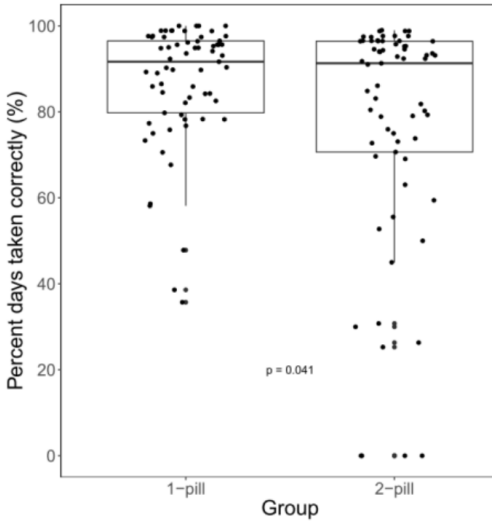
Dual-component SPC (Olmesartan + HCTH, 20/12.5 mg) + Amlodipine 5 mg

HCTH: Hydrochlorothiazide

Together with World Congress of Cardiology

PDT & PDTc





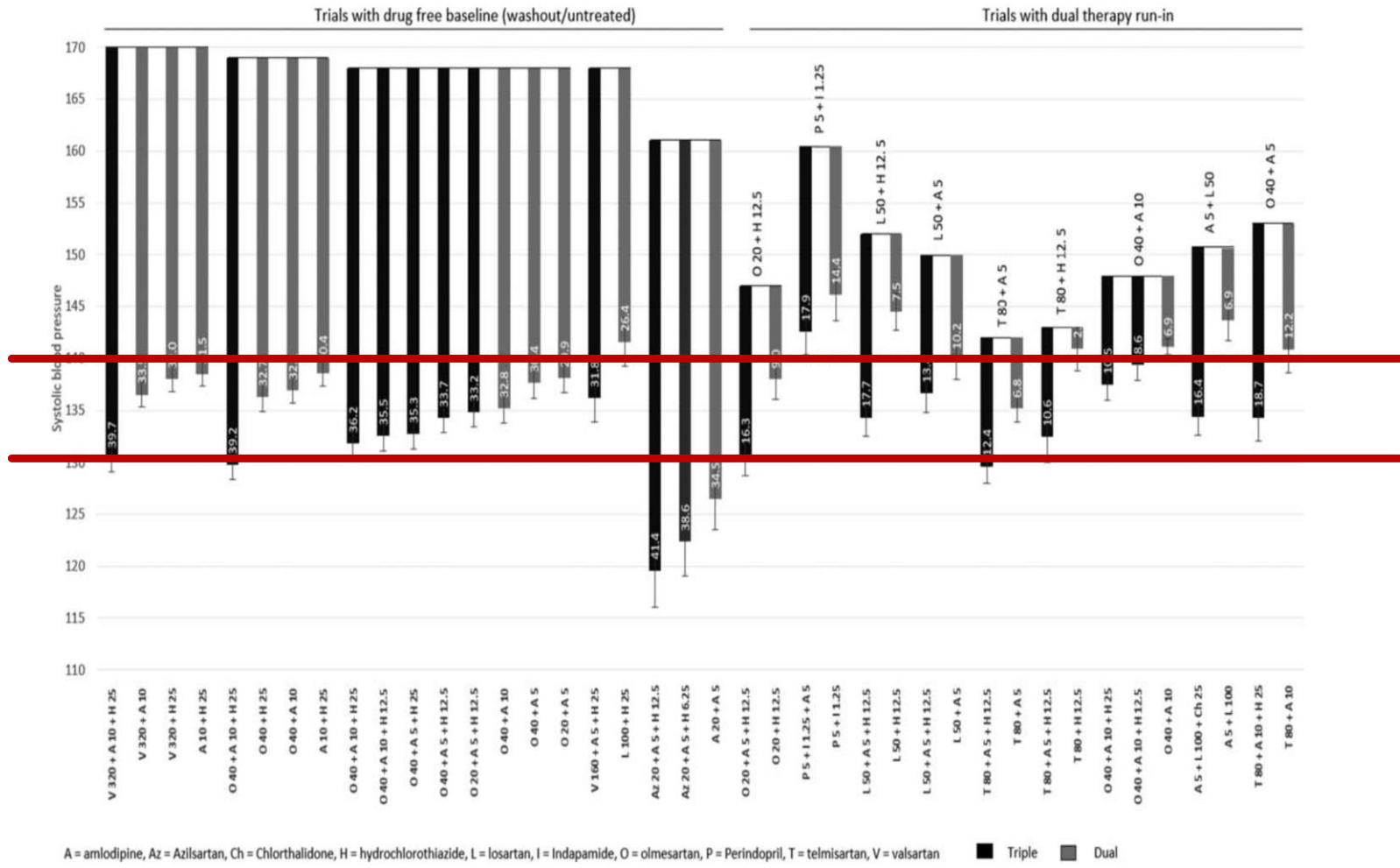
ESC Congress Paris 2019 World Congress of Cardiology

THE AMTRAC STUDY

TRIPPLE THERAPY

“4 TIMES

MORE EFFECTIVE”



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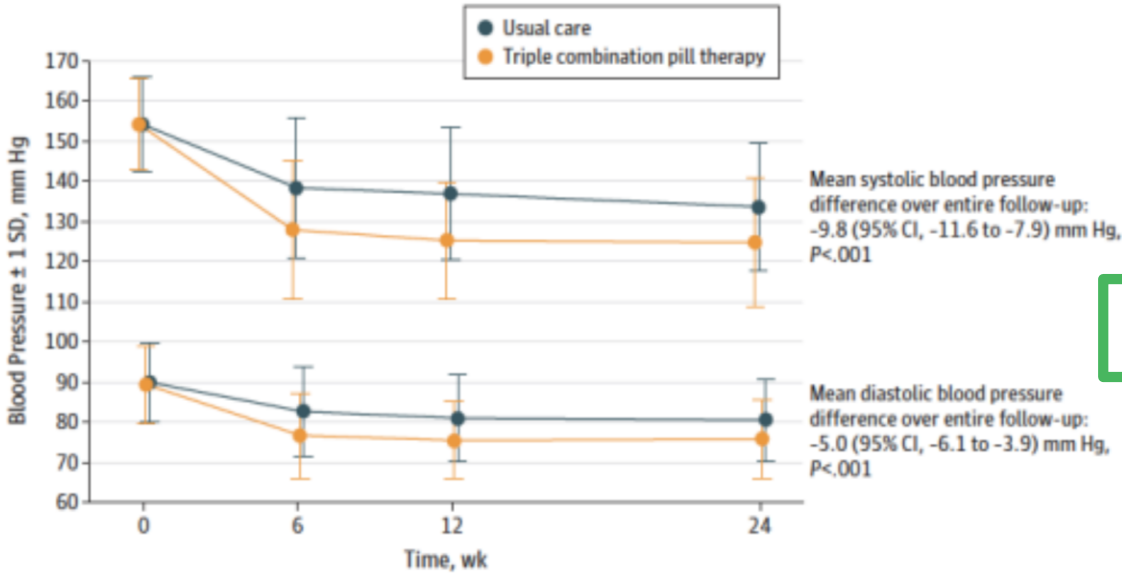
Salam A, Journal of Hypertension.2019

Fixed low dose triple therapy combination as initial therapy for mild-moderate hypertension

700 randomized patients (mean age, 56 yrs; 58%women; 29% diabetes)
mean baseline BP 154/90mmHg
Once-daily low-dose fixed-dose triple combination pill (20mg telmisartan, 2.5mg amlodipine, 12.5mg chlorthalidone) versus usual care
Primary outcome: Proportion achieving BP target BP (<140/90mmHg or <130/80mmHg in patients with diabetes or CKD) at 6 months



Group	SBP mmHg at 6 months	DBP mmHg at 6 months
Triple Combo	125	76
Usual Care	134	81

Webster R, et al JAMA 2018

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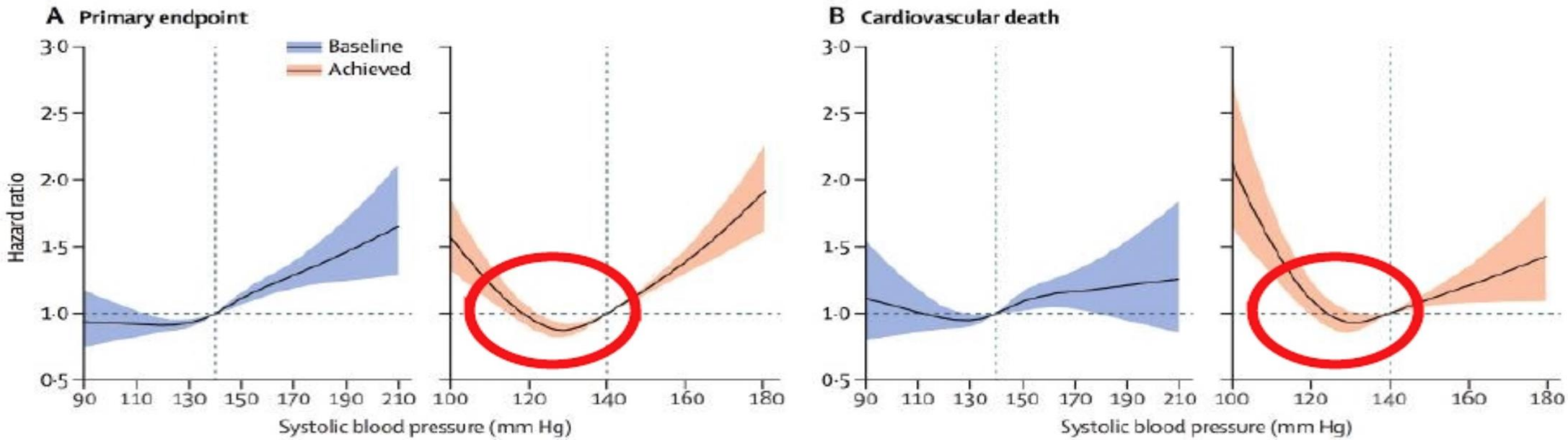
04

THE ELDERLY

Achieved blood pressure and cardiovascular outcomes in high-risk patients: results from ONTARGET and TRANSCEND trials

Michael Böhm, Helmut Schumacher, Koon K Teo, Eva M Lonn, Felix Mahfoud, Johannes F E Mann, Giuseppe Mancia, Josep Redon, Roland E Schmieder, Karen Sliwa, Michael A Weber, Bryan Williams, Salim Yusuf



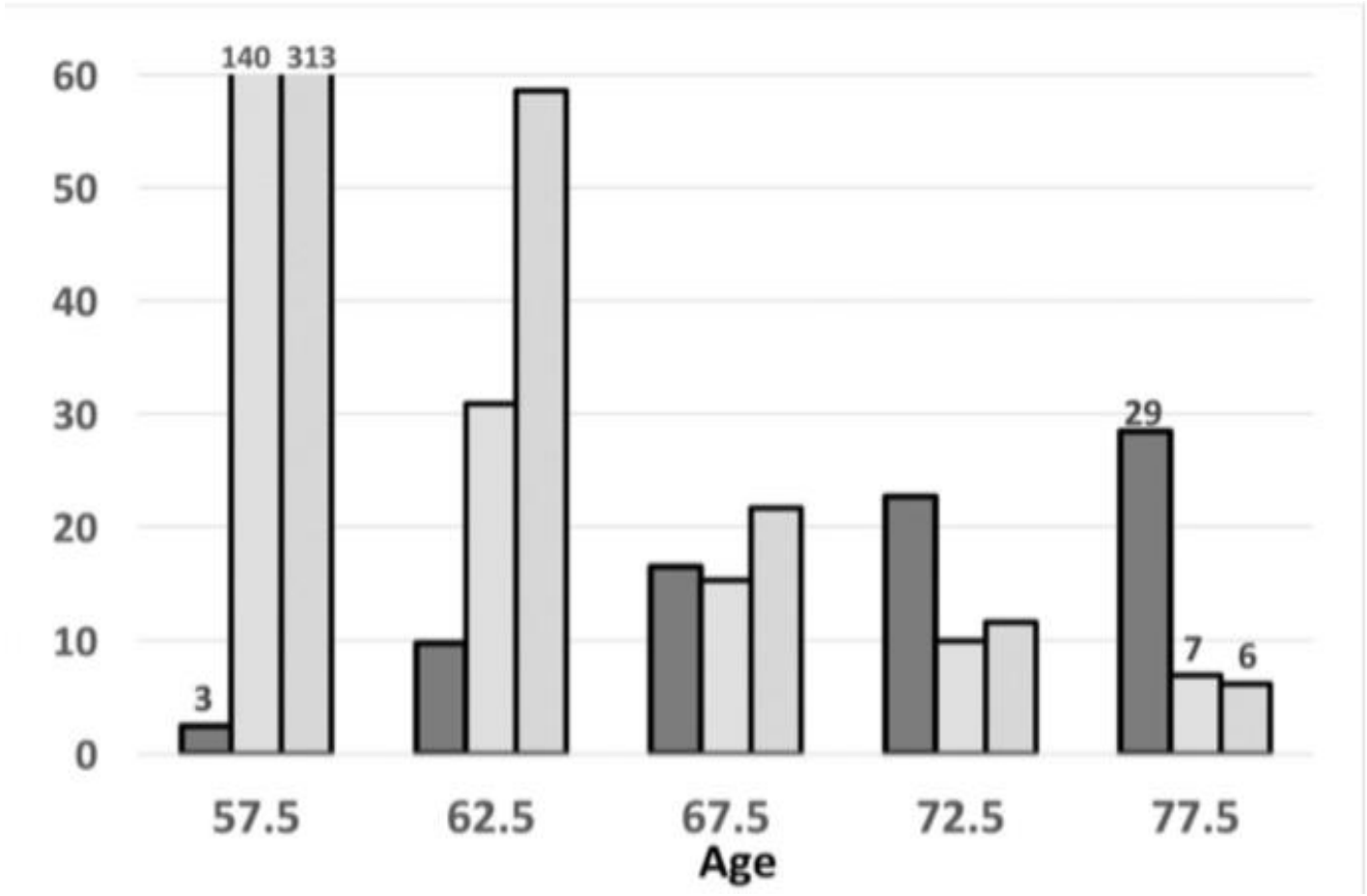
ESC Congress
Munich 2018

Baseline
Achieved

Böhm et al, Lancet 2017

AGE-DEPENDENT RISK REDUCTION

- More risk reduction
- Less NNT



Roush GC. J Hypertense 2019

SPRINT IN NUMBERS

167 NNT to prevent 1 CV death

83 NNT to prevent all-cause death

56 NNH to cause 1 case of AKI or renal failure

42 NNH to cause 1 SAE

THE ELDERLY?

- Comorbidity
- Polypharmacy
- Frailty
- Life expectancy
- Cognitive function
- Lifestyle modification

Ngoc Thanh Van Nguyen. E-Jour Cardio Prac 2019

Changing paradigm in hypertension management

THANK YOU FOR YOUR ATTENTION

NGOC THANH VAN NGUYEN, MD

NTCC 2019, HCMC