



Role of fixed combination therapy in multiple risk patients:

Telmisartan HCTZ

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Monotherapy in patients without DM, CAD, CHF

- **A (rather) simple choice**
- **one of 5 drug classes (with 1- 4 doses)**
- **≈ 20 possibilities**

However...

- 2/3 of patients will need >1 drug
- Combination therapy
 - ↓ complexity of choice
 - ↑ patient compliance



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Monotherapy titration

- Adverse effects are dose-dependent
- Proper effects of most drugs in monotherapy come with higher dose

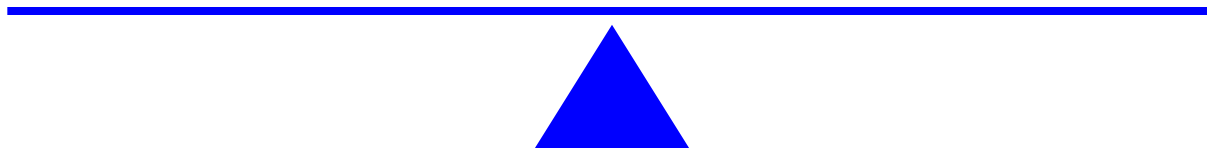
Monotherapy titration



benefit



adverse effects

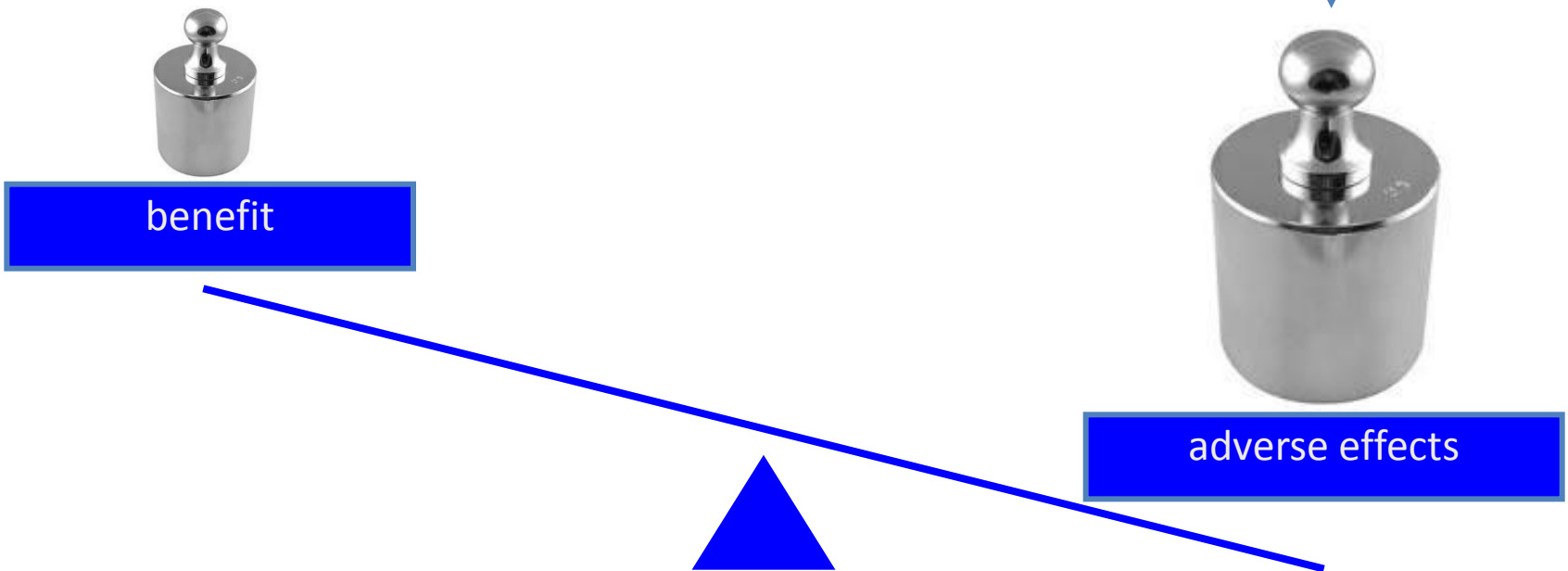




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Monotherapy titration

Monotherapy titration





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Combination therapy

- no dose increase → less adverse effects
- better effect

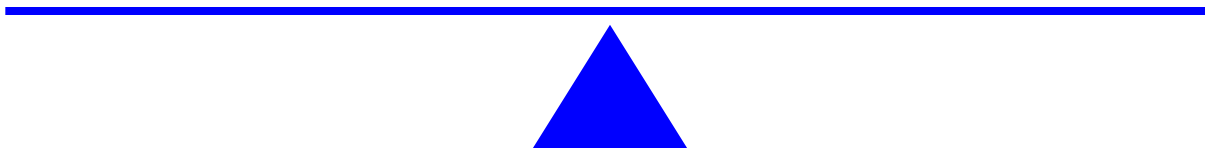
Combination



benefit



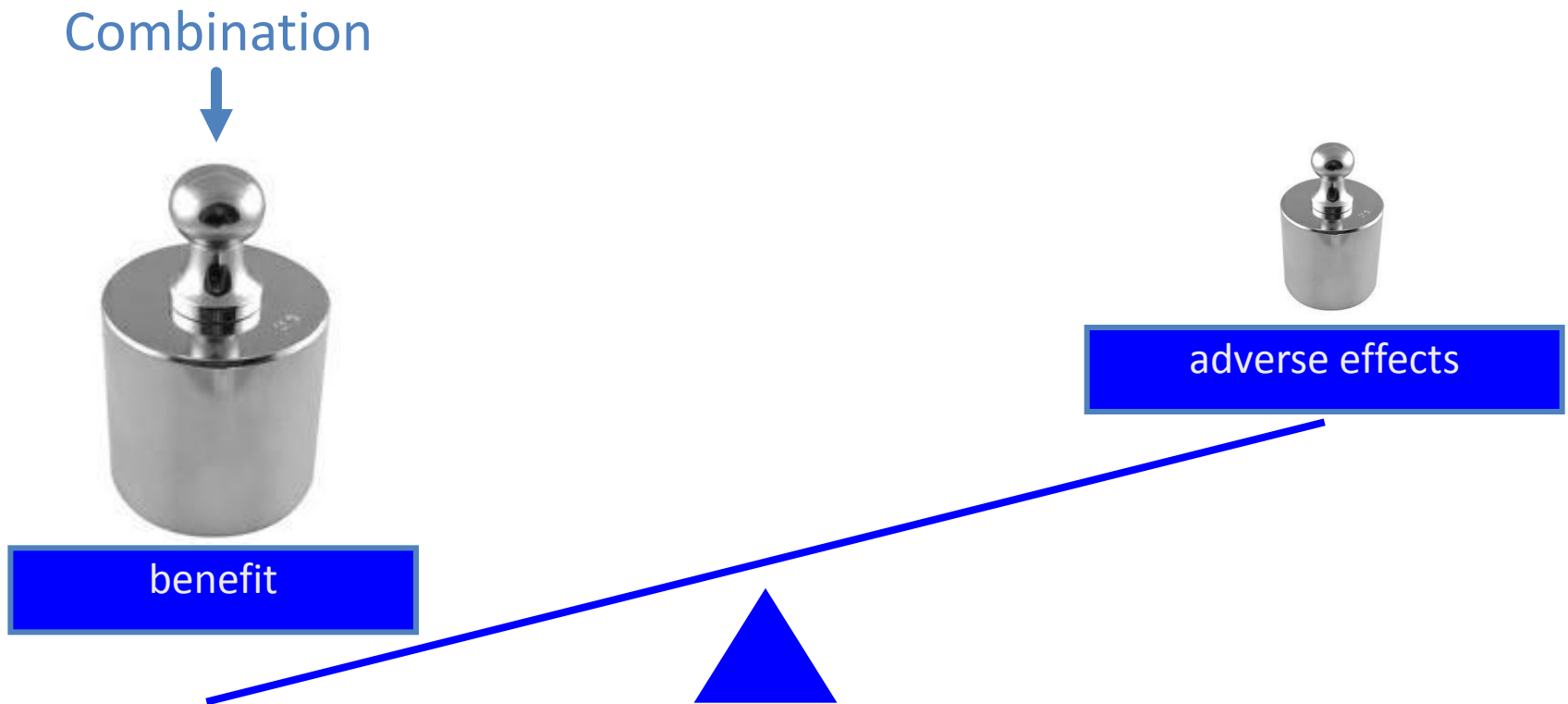
adverse effects





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Combination therapy





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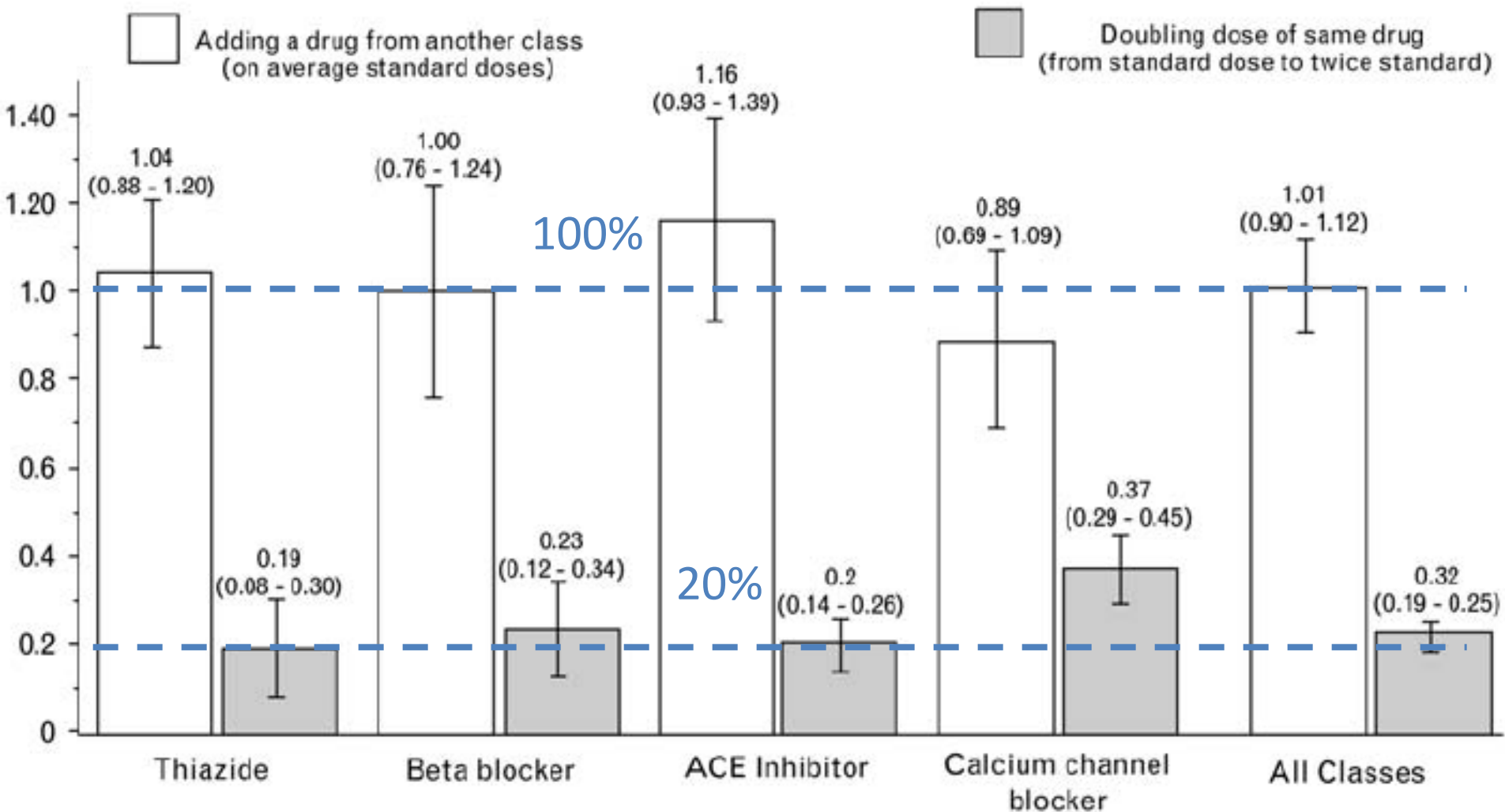
Monotherapy titration vs combination therapy

- **10.968 patients in 42 studies**
- **antihypertensive effect:**
 - doubling dose: **↑ 20%** effect
 - combination therapy: **↑ 100%** effect



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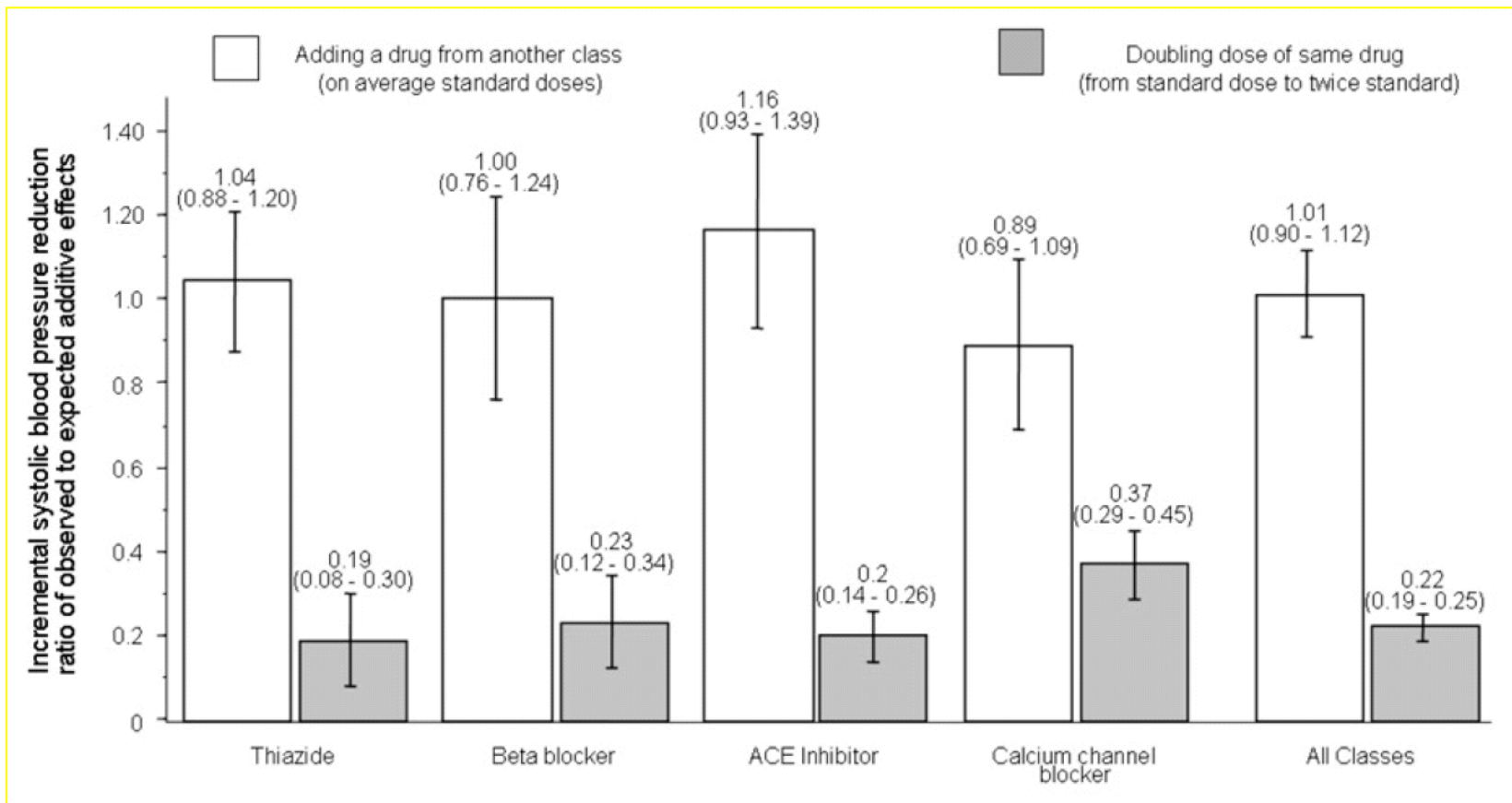
Monotherapy titration vs combination therapy





Ratio of observed to expected incremental blood pressure-lowering effects of adding a drug or doubling the dose according to the class of drug

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Are adverse effects common / important?

- review of 354 studies
- administering $\frac{1}{2}$ of standard dose reduces the incidence of adverse effects by:
 - CCB: ↓ 81% (peripheral edema)
 - thiazids: ↓ 80% (hypokalaemia)
 - BB: ↓ 27% (bradycardia / fatigue)



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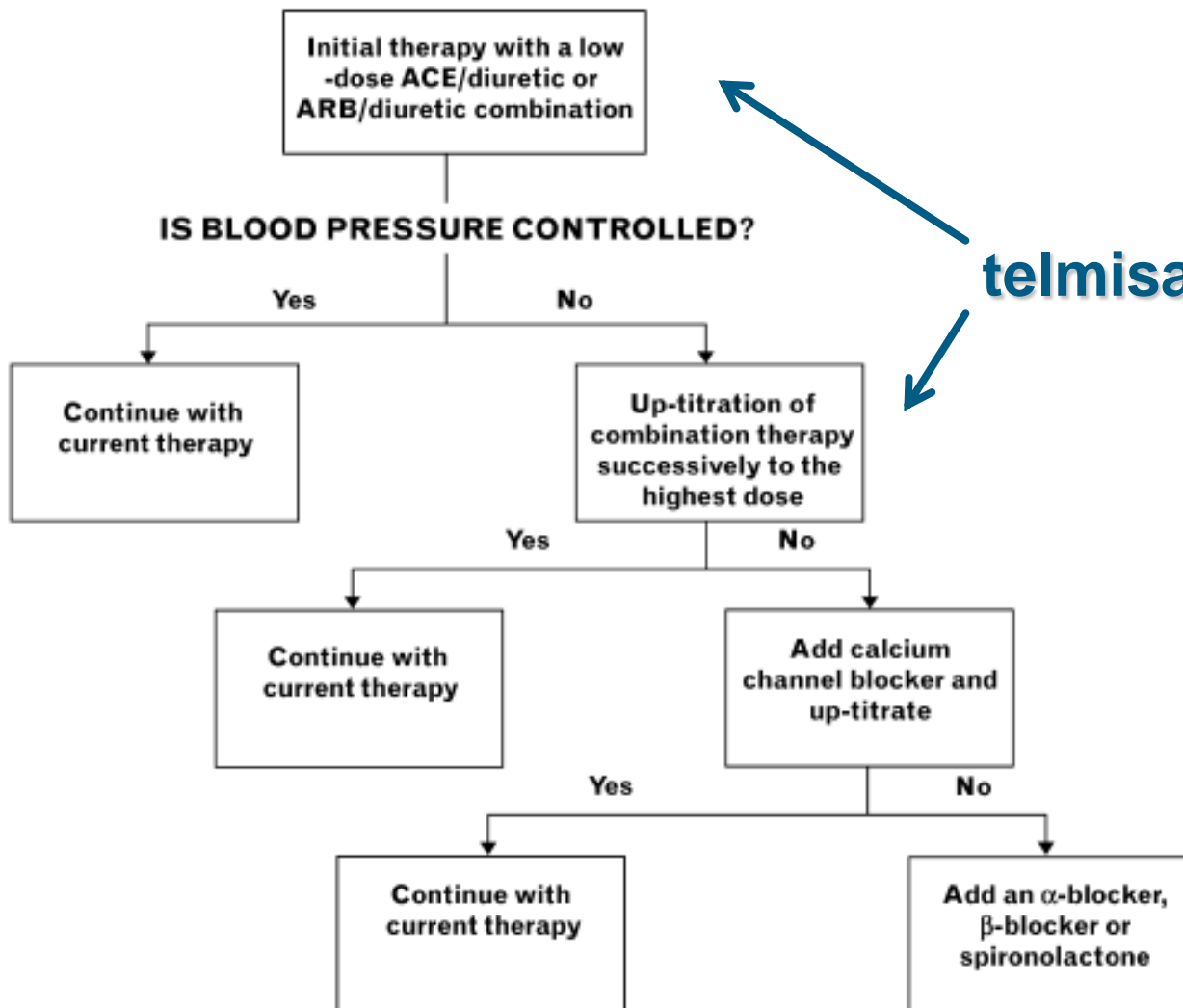
Advantages of FIXED combinations

- How many options for patients requiring 3 medications ?
- based on pure mathematics (only for the “strong” 5!):
 - 6 different CCB; 16 possible starting doses
 - 5 different diuretics; 8 possible starting doses
 - 5 different BB; 11 possible starting doses
 - 7 different ACEI; 16 possible starting doses
 - 6 different ARB; 11 possible starting doses
- three prescription scenarios and number of possibilities:
 - 1 dose / drug ~ **3000**
 - lowest and middle dose / drug; sequence not important ~ **35.000**
 - lowest and middle dose / drug; sequence IS important > **200.000!**



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Simple algorithms with fixed combinations



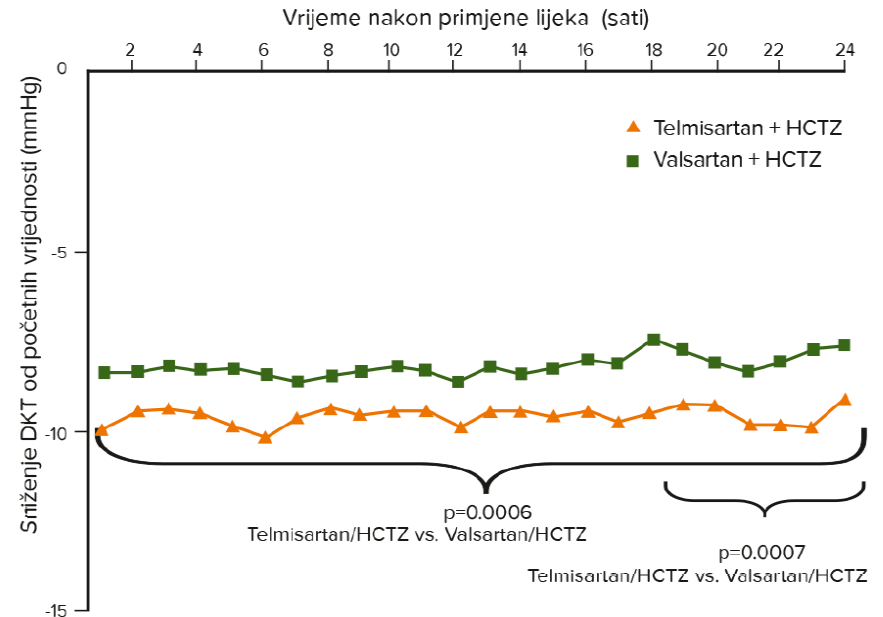
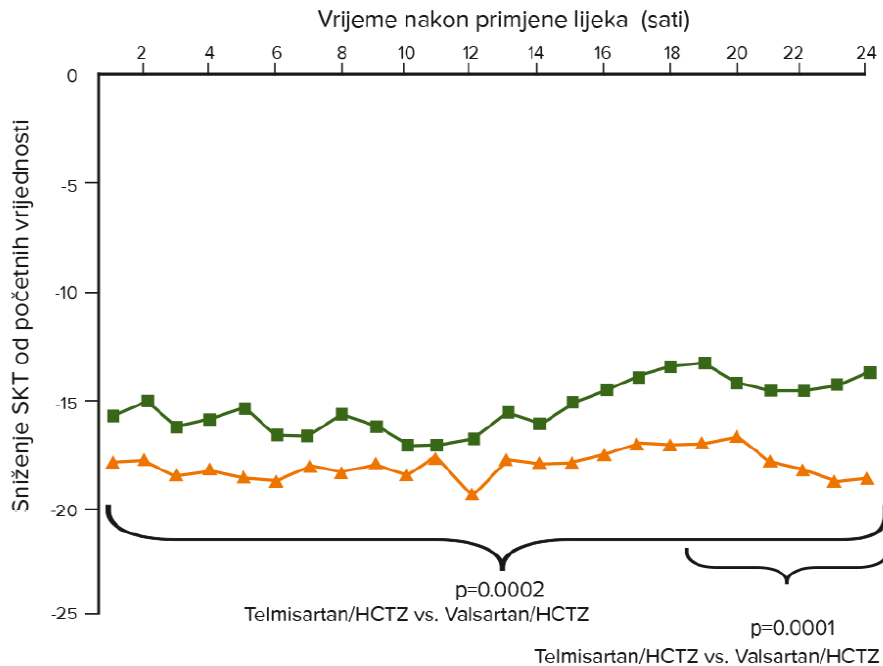
telmisartan + HCT





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Telmisartan HCT in 24 h efficacy

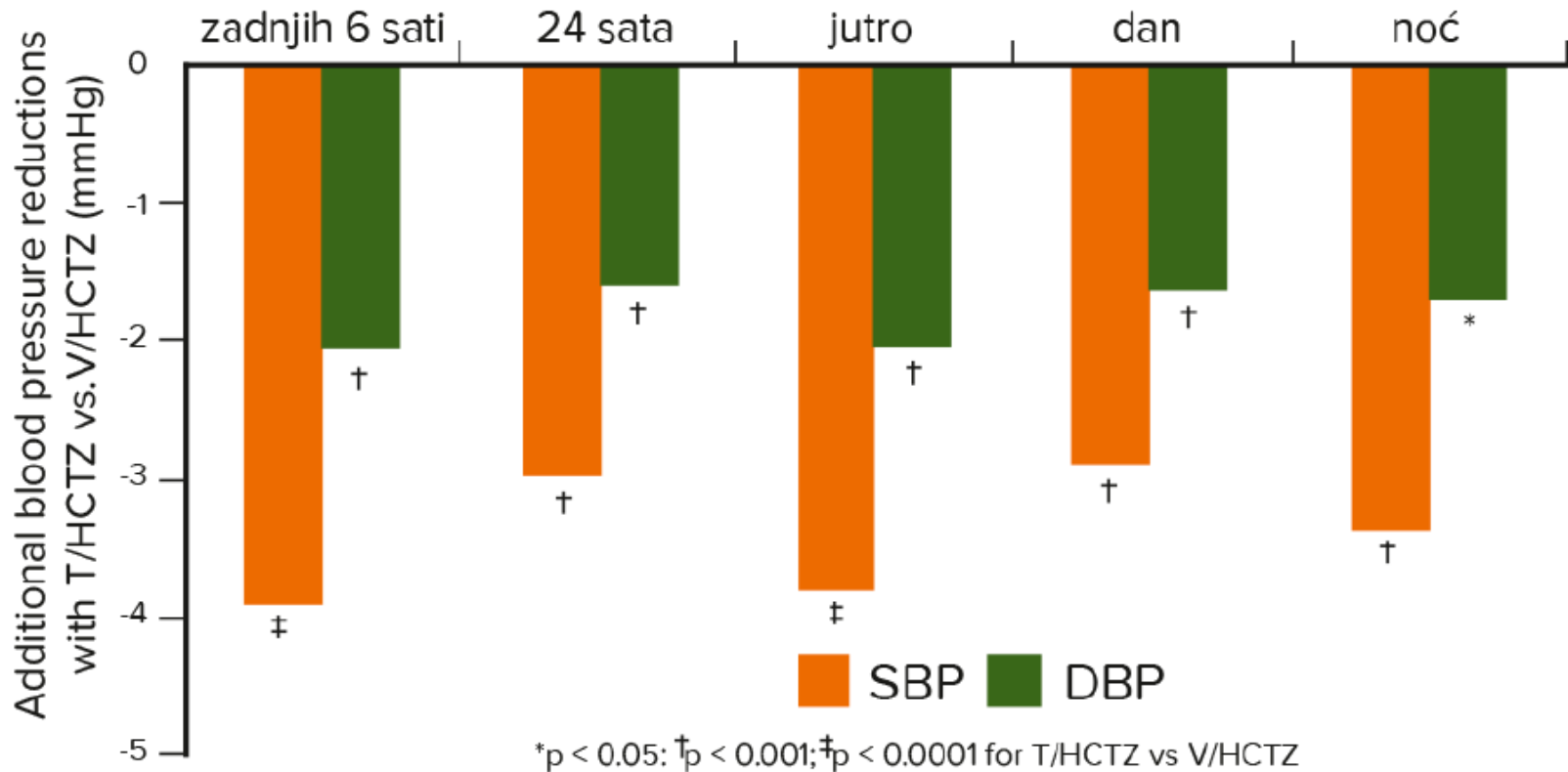


- 🕒 Efficacy in BP lowering vs valsartan is continuously higher during 24hour period
- 🕒 Significantly stronger in last 6 hours period



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Telmisartan HCT in 24 h efficacy



- 🕒 Significant differences in BP lowering vs valsartan
- 🕒 Each mmHg brings multi-fold benefits



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Conclusion

In high-risk, overweight/obese patients with hypertension and type 2 diabetes,

- **T/HCTZ provides significantly greater BP lowering versus V/HCTZ**
- **throughout the 24-hour dosing interval,**
- **particularly during the hazardous early morning hours.**



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Telmisartan HCT in ISH

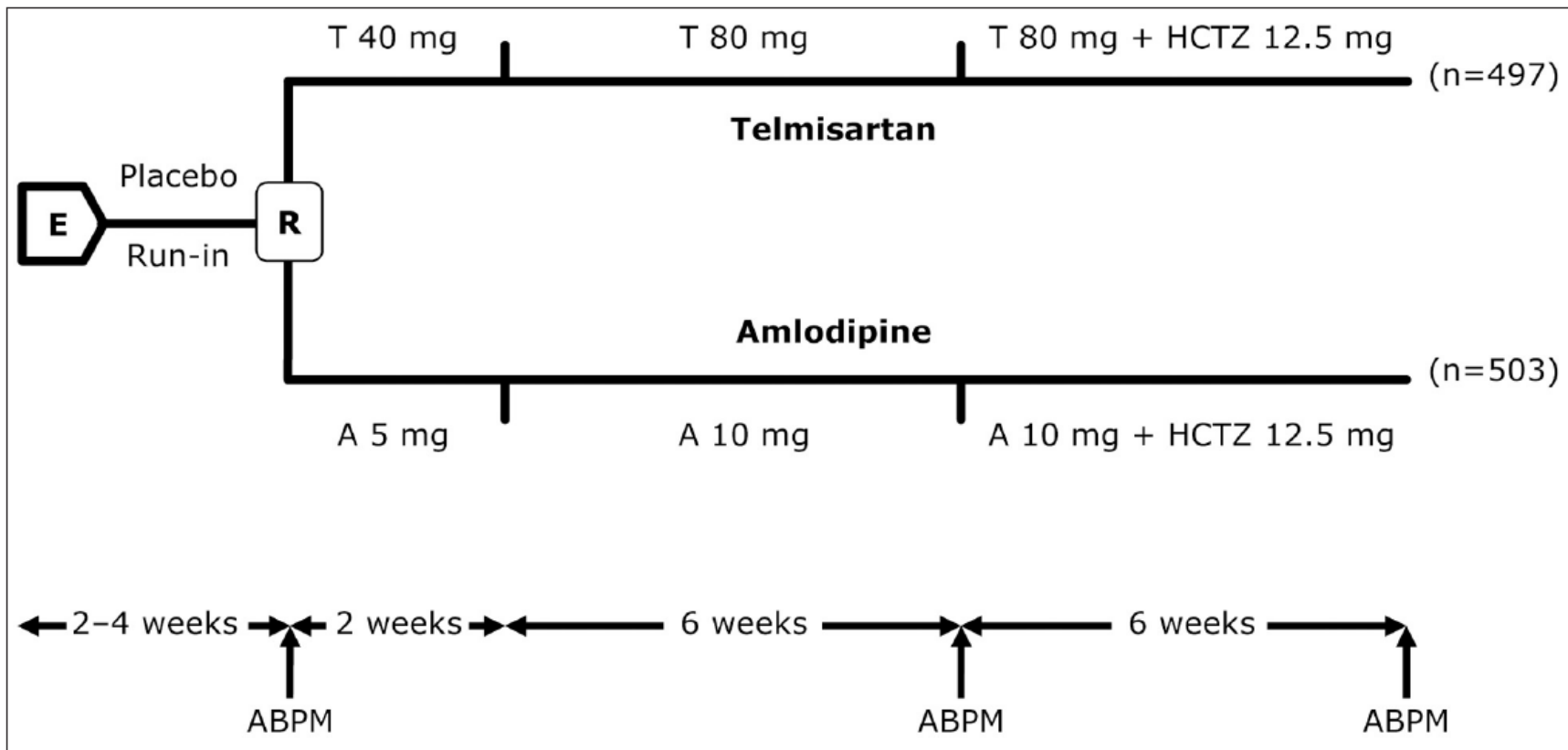
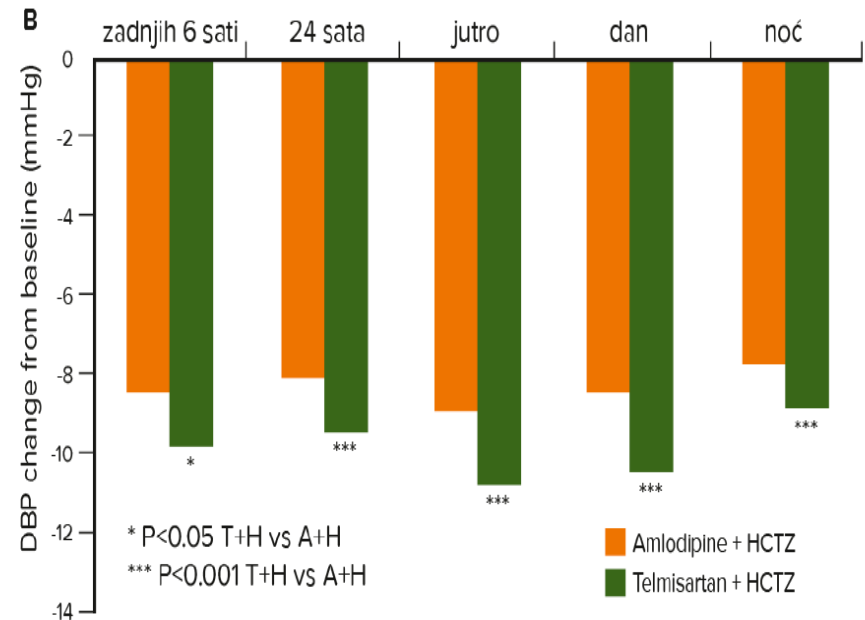
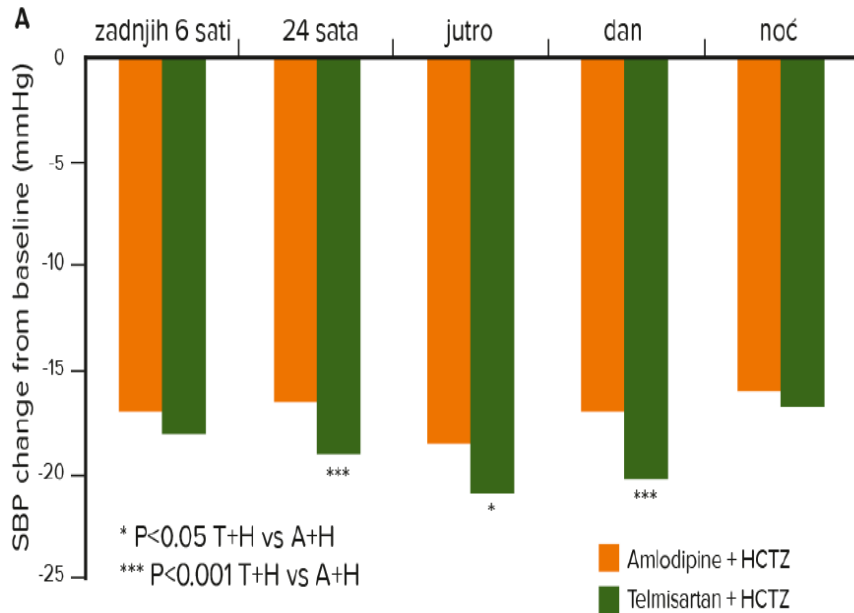


Figure 1. Study design. E=entry; R=randomization; T=telmisartan; HCTZ=hydrochlorothiazide; A=amlodipine; ABPM=ambulatory blood pressure monitoring



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Telmisartan HCT in ISH



Efficacy in BP reduction higher during 24 h vs amlodipin



Sinergistic effect of 2 agents with different mode of action



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Telmisartan HCT safety

Table II. Number of Patients (n [%]) With Adverse Events Reported With an Incidence of $\geq 2\%$ in Either Group at Any Stage of the Trial

	TELMISARTAN (\pm HCTZ) (N=497)	AMLODIPINE (\pm HCTZ) (N=503)
Total	205 (41.2)	270 (53.7)*
Related to study drug	40 (8.0)	168 (33.4)*
Discontinued due to adverse events	25 (5.0)	57 (11.3)*
Adverse events reported		
Peripheral edema	6 (1.2)	122 (24.3)*
Edema	1 (0.2)	22 (4.4)
Headache	15 (3.0)	13 (2.6)
Dizziness	15 (3.0)	7 (1.4)
Vertigo	12 (2.4)	6 (1.2)
Bronchitis	8 (1.6)	10 (2.0)
Flushing	0 (0.0)	11 (2.2)

HCTZ=hydrochlorothiazide; * $p < 0.0001$, telmisartan vs. amlodipine



Patient adherence to therapy is crucial !



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Conclusion 1

- The significantly superior SBP reductions with T+H during the morning and daytime periods, **provided a significantly ($p < 0.0001$) larger mean reduction with T+H for the 24-hour period as a whole**
- **The greater reductions in BP** seen in our study with T+H compared with A+H **are likely due to differences between the mechanism of action of telmisartan and HCTZ.**
- CCBs, on the other hand, have intrinsic natriuretic properties and are thus **less likely to provide additive benefits from combination with HCTZ**
- Therefore, **patients with isolated SH may benefit from initial treatment with Telmisartan+H combination therapy**



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Conclusion 2



- **Let's make ours and patient's life simpler and easier !**



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Thank you