Recommendation 10

Should adult patients with high initial systolic blood pressure ≥160 and/or diastolic blood presuure ≥100 be offered as initial therapy <u>any combination treatment</u> compared with any monotherapy?

In patients with hypertension, the guideline panel recommends ……			
Population	Adult patients with confirmed hypertension with blood pressure equal to or higher than 160/100 mmHg.		
Intervention	Combination pharmacotherapy		
Factor	**Decision**	**Explanation**	
High or moderate evidence *(is there high or moderate quality evidence?)* The higher the quality of evidence, the more likely is a strong recommendation.	□ Yes □ No		There is no direct evidence that the use of initial combination therapy is more effective in reducing the clinical outcomes compared to the step-up regimens. There is moderate quality evidence that an initial combination treatment and tight uptitration sequence achieves better BP control (64.7% versus 52.7%; RD 12.0%; 95% CI: 1.5% to 22.4%; P=0.026 at 6 months). There is good quality evidence from multiple RCT-s that, compared to monotherapy: – combination therapy achieves greater BP reductions and control rates; – at least 2/3 of patients (including stage 1 hypertension) need combination therapy to achieve BP control; – combination therapy with moderate doses of 2 drugs is no more harmful than monotherapy and may reduce specific adverse effects of e.g. CCB-s. There is good quality evidence from a meta-analysis that the extra BP reduction from combining

			drugs from 2 different classes is approximately 5 times greater than doubling the dose of 1 drug. There is good quality evidence froma meta-analysis that the greater effect of combination treatment on BP is seen also in Stage 1 hypertension. We did not find any meta-analysis investigating the possible superiority of predefined combinations as initial treatment in reducing cardiovascular events. Therefore, there exist no combination that can be currently considered superior to all others. Some RCT-s have been performed focusing on the superiority of certain combinations compared to others: - a calcium channel blocker+diuretic regimen was shown to be inferior to other combinations for preventing myocardial infarction (odds ratio 1.98, 95% confidence interval 1.37—2.87) but not stroke; - an ACEI (or ARB)+diuretic combination was not significantly superior for stroke and myocardial infarction prevention compared with diuretic+beta blocker; - ACCOMPLISH trial (moderate quality evidence) demonstrated that starting a CCB+ACEI in high-risk hypertensive patients significantly reduced the primary composite outcome (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, hospitalization for angina, sudden cardiac arrest, coronary revascularization) by 20% compared with ACEI+HCTZ).

Certainty about the balance of benefits versus harms and burdens *(is there certainty?)* The larger the difference between the desirable and undesirable consequences and the certainty around that difference, the more likely a strong recommendation. The smaller the net benefit and the lower the certainty for that benefit, the more likely is a conditional/ weak recommendation.	□ Yes □ No		There is no certainty that the use of initial combination therapy compared to well-conducted step-up strategy will lead to better clinical outcomes. There is moderate level of certainty that the harms of combining reasonable doses of current BP lowering agents are not significantly higher than of monotherapy. There is no information on frail patients.

Certainty in or similar values *(is there certainty or similarity?)* The more certainty or similarity in values and preferences, the more likely a strong recommendation.	□ Yes □ No		The panel assumes that patients place more value .... and less value ....
Resource implications *(are the resources worth the intervention?)* The lower the cost of an intervention compared to the alternative that is considered and other costs related to the decision – that is, the less resources consumed – the more likely is a strong recommendation.	□ Yes □ No		
Overall strength of recommendation (*consider the extent to which one can be confident that adherence will do more good than harm)*	**Net benefits** = the intervention clearly does more good than harm. **Trade-offs** = there are important trade-offs between the benefits and harms. **Uncertain trade-offs** = it is not clear whether the intervention does more good than harm. **No net benefits** = the intervention clearly does not do more good than harm.		