PICO question 9: What target BP should pharmacologic treatment aim to achieve?

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE/PANEL INPUT
VALUES	**Is there important uncertainty or variability about how much people value the main outcomes?**	Important uncertainty or variability ☐ / Possibly important uncertainty or variability ☒ / Probably no important uncertainty or variability ☐ / No important uncertainty or variability ☐ / No known undesirable outcomes ☐ **Detailed judgements**	**PANEL INPUT** From a patient perspective, HTN is often a silent disease and patients may not take antihypertensive medications as directed because their positive effects are not as obvious as potential side-effects from the medications.[4] Society and patients want to avoid premature mortality or disability. Serious adverse events are feared also, but their duration and severity are often not well characterized in trials. Asymptomatic condition with short-term lack of direct signs of benefit is an issue for retaining patients in care and maintaining medication adherence.
BENEFITS AND HARMS OF THE OPTIONS	**What is the overall certainty of the evidence of effects?**	No included studies ☐ / Very low ☐ / Low ☐ / Moderate ☒ / High ☐ **Detailed judgements**	**RESEARCH EVIDENCE** Desirable/undesirable effects per 1000: 130 vs 140: 17 fewer HF and stroke but 20 more AE; 120 vs 130-139: 27 deaths, 1 more AE. In patients with comorbidity (CAD, DM, CKD): consistent benefit with lower targets (variable thresholds). The benefit is the final reduction in CV events, reaching WHO NCD targets. AE includes dizzziness in intensive control group. Lower targets can increase ischemia in patients with CAD. With lower BP target and older age the tradeoffs can shift towards larger harms. Lower target will be associated with less adherence. **PANEL INPUT** Summarizing evidence for "intensive versus standard" BP treatment targets is challenging – generalizing low and high across differently designed RCTs leads to heterogeneity; dividing up trials into specific targets leads to small numbers and imprecision. Summary results from the Murad[66] meta-analysis leads to the conclusion that treatment to a lower BP target in older individuals leads to a significant reduction in all-cause and CVD mortality, CKD, MI, or stroke outcomes. Despite using different trials and evidence synthesis approach, the Reboussin (ACC/AHA guideline reference 3) review yielded similar results.[46] Neither of these meta-analyses account for the very high risk of the trial cohorts reviewed – at least for SPRINT and ACCORD.[67] [68] We caution against applying this evidence to lower risk patients with raised BP or HTN – specifically, those not meeting eligibilty criteria for SPRINT, ACCORD, or SPS3.[69] Questions
	How substantial are the desirable anticipated effects?	Don't know ☐ / Trivial ☐ / Small ☐ / Moderate ☐ / Large ☒ / Varies ☐ **Detailed judgements**	
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	Do the desirable effects outweigh the undesirable effects?	No ☐ / Probably No ☐ / Don't know ☐ / Probably Yes ☐ / Yes ☒ / Varies ☐ **Detailed judgements**	

			about exclusion of frail elderly in these trials persist, though SPRINT did arguably include older and frail elderly ppts. Small sample size meant uncertainty in detecting differences in this overall finding by age, diabetes, or CKD status. Nonetheless, there was no clear difference by age 65–74 vs ≥75 years. Network meta-analyses found a similar direction of effect but more optimistic effect sizes regarding intensive treatment benefit.[70] [71]
RESOURCE USE	**How large are the resource requirements?**	Large costs ☐ Moderate costs ☒ Small ☐ Moderate savings ☐ Large savings ☐ Varies ☐ **Detailed judgements**	Intensive BP treatment in the SPRINT trial meant one additional medication, one additional office visit, and one additional laboratory test evaluation on average, and additional titration visits per participant over 3.25 years, compared with standard treatment. This translates to about USD 13 000 more per patient over their remaining lifetime.[72] [73] Costs are much less in countries other than US (SPRINT). Treating to lower targets will have diminishing returns as the magnitude of benefit becomes smaller and shifts focus to a smaller number of patients.
	How large is the incremental cost relative to the net benefit?	Very large ICER ☐ Large ICER ☐ Moderate ICER ☒ Small ICER ☐ Savings ☐ Varies ☐ **Detailed judgements**	A cost-effectiveness study of screening and optimal management of HTN and DM and CKD in an Australian setting found that an intensive management of previously uncontrolled HTN compared with usual care resulted in an ICER of AUD 2588 (Australian). They do not specify the target BP for the comparisons.[74] SPRINT trial analysis provides similar inferences.[73] [74]

EQUITY	**What would be the impact on health inequities?**	Increased ☐ Probably increased ☐ Uncertain ☐ Probably reduced ☒ Reduced ☐ Varies ☐ **Detailed judgements**	**RESEARCH EVIDENCE** HTN is a "disease of poverty", at least in some countries. Even using the <140/90 goal, "many barriers in access to HTN care in low-income settings are low patient health literacy; overburdened health-care providers; the lack of an organizational structure to accommodate a nonphysician as a primary care provider; the lack of confidence and/or policy towards the nonphysician providers' ability to manage uncomplicated and stable patients; the lack of infrastructure for data collection and monitoring of clinical information on a periodic basis as a more intensive target seems to requires more data collection and monitoring; and finally, limited resources."[21] **PANEL INPUT** Focus on intensifying treatment in patients already under care and with lower BP but not if goal may divert attention and resources away from treating people who are unaware/untreated/uncontrolled – the result could be exacerbating inequities in health outcomes. Treating BP can reduce equity because preventing CV events reduces mortality in the society in general. Uncontrolled HTN might be over-represented in vulnerable populations. So, improving HTN treatment and control through better treatment and lower BP targets could reduce inequality in the long term. It varies based on the budget and whether it is fixed. In an overloaded health system, standard of care may suffer. In a well-resourced system, it will be easier. This is an opportunity to expand access and resources and look at models other than physician-centric ones.

ACCEPTABILITY	**Is the option acceptable to key stakeholders?**	No ☐ Probably No ☐ Uncertain ☐ Probably Yes ☒ Yes ☐ Varies ☐ **Detailed judgements**	**RESEARCH EVIDENCE** Acceptable to health care systems and providers in principle, yes, though governments and health systems are often distracted by more acute demands and higher priority placed on acute conditions and health emergencies. Investment in the primary health care platform required for effective HTN management is often a challenge. Countries with low rates of HTN control using more conservative BP thresholds may feel burdened by any request to set more ambitious BP treatment goals, even if in selected high-risk patients. Many well-known barriers to access to HTN care in low-income settings exist.[22] **PANEL INPUT** Intensive treatment for selected patients adds complexity for health workers; emphasis on team-based care in low-resource settings means that simple, protocolized care is needed. Intensive treatment for some patients complicates treatment protocols and may lead to decisional overload, especially for health workers with more limited training and/or autonomy. On the other hand, strict targets in the general public are less acceptable to stakeholders. Most available evidence is from high-risk patients receiving intensive treatment and not from the general public. Patients may find more intensive treatment for a chronic asymptomatic condition unacceptable. Taking one additional medication on average may lead to more side-effects (even if not serious AEs), may lead to more out of pocket medications costs, and may lead to the inconvenience of more office visits. People at risk have likely been seen in various settings and are better informed.

FEASIBILITY	**Is the option feasible to implement?**	No ☐ Probably No ☐ Uncertain ☐ Probably Yes ☒ Yes ☐ Varies ☐ **Detailed judgements**	If risk stratification was not easy, implementation becomes difficult. A few countries in the world have good control, which suggests that it is not feasible. Intensive BP treatment requires more resources and should be the goal of HTN programmes that are already achieving control <140 across the entire population. Risk of concentrating resources on the "high achiever" patients and providers is a concern. From Risso, 2015: The guidelines envisage that all clinics should manage patients with HTN, with staff undergoing specific training in screening and HTN management. BP is not routinely checked during attendance at primary care clinics for other problems, contrary to national guidelines; however some doctors do measure BP in all patients visiting the clinics.[4] Additional evidence of feasibility can be inferred from the WHO, Resolve to Save Lives initiative that included improving the control of HTN using the WHO HEARTS technical package. Five components are necessary for a successful HTN control programme: drug- and dose-specific treatment protocols; access to quality-assured medications and BP monitors; team-based care; patient-centred care delivered in the community, and information systems to enable quality improvement. This programmatic experience of protocol-based treatment of more than 3 million persons from 18 countries was done over a short period.[75]

Recommendation 6: target blood pressure

Recommendations	**WHO recommends a target BP treatment goal <140/90 mmHg in all patients with hypertension without comorbidities.** **WHO recommends a target systolic BP treatment goal <130 mmHg in patients with hypertension and known CVD** **WHO suggests a target systolic BP treatment goal <130 mmHg in high risk patients with hypertension (those with high CVD risk, diabetes, chronic kidney disease).**				
Type of recommendation	We recommend against the option or for the alternative	We suggest not to use the option or to use the alternative	We suggest using either the option or the alternative	We suggest using the option	**We recommend the option**
	☐	☐	☐	☐	☒
Justification	Trial evidence is convincing, but feasibility, equity, opportunity cost considerations count against a recommendation to pursue intensive BP treatmen in all jurisdictions..				
Subgroup considerations	• Lack of statistical power to define RR in subgroups, including DM, CKD • No interaction between "old" (65–74) and "very old" (75+) in Murad[66], potentially due to lack of power. • Because some of the major intensive BP treatment trials reviewed selected patients based on high risk (SPRINT, ACCORD, SP3), caution is needed regarding extrapolating these findings to the general population or even intermediate CVD risk groups.				
Implementation considerations	Intensive BP in selected high-risk patients is more justified in countries, subnational areas, or health systems with demonstrated success in controlling BP <140/90 mmHg in the general population living with HTN. Considering the failure of most nations and health care systems to reach population HTN control goals of >50% controlled <140/90 mmHg, putting a priority on intensive treatment in high-risk patients risks focusing more effort on high-risk people when many moderate-risk people are untreated or treated but uncontrolled. The latter are more likely younger and in their productive years, supporting families. Our contention is that intensive BP treatment is "extra credit" and not the main goal. European guidelines frame this prioritization better than US guidelines. Intensive treatment for selected patients adds complexity for health workers; emphasis on team-based care in low-resource settings means that simple, protocolized care is needed. Intensive treatment for some patients complicates treatment protocols and may lead to decisional overload and the potential for therapeutic inertia, especially for health workers with more limited training and/or autonomy.				

Monitoring and evaluation considerations	More monitoring resources are needed to reach intensive BP goals in terms of number of medications, number of monitoring visits. Trials have not tested the roles of task shifting or out of office/home monitoring in pursuit of more intensive BP goals. A systems approach to programme evaluation will be needed. For example, trials or simulation studies should examine the impact of increased service intensity to achieve intensive treatment for selected high-risk patients on the access to primary care visits and loss-to-follow up among the remainder of HTN patients (who are "not yet" high risk, and likely to be of working age).
Research priorities	• Better to characterize serious AEs in trials of intensive vs standard BP treatment (severity, duration, costs, utilities) • Quantification of the resource commitment required for more intensive treatment in LICs and MICs and consideration of opportunity cost of directing resources away from primary care by focus on achieving <140/90 in all hypertensives to focus on specialized HTN treatment in high-risk patients • Research needed on the feasibility, acceptability, and efficacy of intensive treatment in high-risk LIC and MIC populations • Inclusion of cognitive outcomes in trials (note provocative results from ACCORD and SPRINT in terms of cognitive outcomes) • More implementation research to demonstrate intensive treatment is feasible in real clinical practice.