PICO question 2: Is any laboratory testing necessary prior to initiation or during titration of pharmacological treatments?

	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: [X] Possibly important uncertainty or variability: [ ] Probably no important uncertainty or variability: [ ] No important uncertainty or variability: [ ] No known undesirable outcomes: [ ] **Detailed judgements**	There is no research evidence about how people value performing tests prior to starting pharmacological treatment although intuitively people generally like to have tests performed
BENEFITS AND HARMS OF THE OPTIONS	**What is the overall certainty of the evidence of effects?**	No included studies: [ ] Very low: [X] Low: [ ] Moderate: [ ] High: [ ] **Detailed judgements**	**RESEARCH EVIDENCE** The systematic review did not identify direct evidence to support this question. Indirect evidence demonstrates that 10-30% patients with HTN may have secondary HTN, comorbidities or develop adverse events after treatment (e.g. hyperkalaemia and AKI), thus providing a rationale for testing (i.e. desirable effects). The undesirable effects would be incidental findings on testing (likely not important) but importantly can include delay of treatment with potential for adverse CV outcomes. On balance, desirable effects likely outweigh undesirable effects. **PANEL INPUT** All guidelines mention that basic laboratory tests need to be performed at initial assessment. The rationale would be: 1. to identify secondary HTN 2. to identify comorbidities (e.g., DM, dyslipidaemia) 3. to identify end organ damage (e.g. CKD or LVH) 4. cardiac risk stratification 5. to pre-identify potential adverse events from treatments (e.g. uric acid, abnormal electrolytes) 6. compelling indications to pharmacological treatment It would be highly desirable to have this information as it has a major influence on further investigation for secondary causes, treatment of other CV risk factors, BP goal, and initiation and choice of antihypertensive drugs.
	How substantial are the desirable anticipated effects?	Don't know: [ ] Trivial: [ ] Small: [ ] Moderate: [X] Large: [ ] Varies: [ ] **Detailed judgements**	
	How substantial are the undesirable anticipated effects?	Don't know: [ ] Trivial: [ ] Small: [X] Moderate: [ ] Large: [ ] Varies: [ ] **Detailed judgements**	
	Do the desirable effects outweigh the undesirable effects?	No: [ ] Probably No: [ ] Don't know: [ ] Probably Yes: [X] Yes: [ ] Varies: [ ] **Detailed judgements**	

			However, the question is whether treatment can be initiated before having these tests available. There is almost no data to clarify the position. In the Creole study, only 1% of subjects were excluded from the study based on laboratory values – mainly low eGFR or hypokalaemia (personal communication from lead investigator). When testing for aldosterone/rennin activity, treatment may affects test results. An incidental finding of hyponatraemia would lead to not starting diuretics. However, these issues are uncommon. Level of BP matters although without a consistent direction. Some GDG members argued that a very high level should prompt treatment before labs; whereas others thought that a high BP can signal secondary HTN and may signal towards getting the labs.
RESOURCE USE	**How large are the resource requirements?**	Large costs ☐ Moderate costs ☐ Small ☒ Moderate savings ☐ Large savings ☐ Varies ☐ **Detailed judgements**	**RESEARCH EVIDENCE** The basic cost would be for electrolytes, creatinine, lipogram, glucose, HBA1C, dipsticks urine, and ECG. Cost to the individual are small in comparison to lifelong treatment. For health systems laboratory tests will have substantial impact on the health system due to the high levels of HTN in most communities. This may impact under-resourced communities. However, relative to overall costs of treatment and complications this is relatively small.[6] [24]
	How large is the incremental cost relative to the net benefit?	Very large ICER ☐ Large ICER ☐ Moderate ICER ☐ Small ICER ☒ Savings ☐ Varies ☐ **Detailed judgements**	**RESEARCH EVIDENCE** Unlikely to be cost saving. The incremental costs would be small in relation to overall cost of management of HT and its complications. It is unknown whether this would lead to cost saving. It depends on the type of test. Basic tests are less costly. However, if additional tests like echocardiogram, 24 ABPM monitoring were added this will have substantial impact.[24]
EQUITY	**What would be the impact on health inequities?**	Increased ☐ Probably increased ☒ Uncertain ☐ Probably reduced ☐ Reduced ☐ Varies ☐ **Detailed judgements**	**PANEL INPUT** Lab tests are easier to get in well-resourced settings, but in low-resourced settings mandating them before starting treatment can impede treatment and cause disparities.

ACCEPTABILITY	**Is the option acceptable to key stakeholders?**	No ☐ Probably No ☐ Uncertain ☐ Probably Yes ☒ Yes ☐ Varies ☐ **Detailed judgements**	No clear data to suggest lack of acceptability.
FEASIBILITY	**Is the option feasible to implement?**	No ☐ Probably No ☐ Uncertain ☐ Probably Yes ☒ Yes ☐ Varies ☐ **Detailed judgements**	**PANEL INPUT** This depends on available resources but is likely more feasible in well-resourced settings. It is also more likely to be feasible in a clinical setting as opposed to HTN being managed in a public health setting or non-clinical environment. It can vary based on the health system infrastructure and payment system. The move towards point of care diagnostics can make this more feasible.

Recommendation 2: laboratory testing

Recommendation 2	**When starting pharmacologic therapy for hypertension, WHO suggests obtaining tests to screen for comorbidities and secondary hypertension, but only when testing does not delay or impede starting treatment.**				
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	Performing tests will assist in evaluating the following, which is an essential clinical component of the assessment and management of HTN: 1. Identifying secondary HTN 2. Identifying comorbidities (e.g., DM, dyslipidaemia) 3. Identifying end organ damage (e.g. CKD or LVH) 4. Cardiac risk stratification 5. Pre-identifying potential adverse events from treatments (e.g. uric acid, abnormal electrolytes) 6. Compelling indications to pharmacological treatment				
Subgroup considerations	In patients with a history or exam findings that suggests being at high risk for comorbidities or who have severe HTN, testing and detailed assessment are more justified.				
Implementation considerations	Suggested laboratory tests include electrolytes, creatinine, lipogram, glucose, HBA1C, dipsticks urine, and ECG. In low-resourced areas or non-clinical settings where testing may not be implementable because of additional costs, access to laboratories and ECG, treatment should not be delayed and testing could be arranged to be done subsequently. Some meds like long-acting dihydropyridine CBB are more amenable to being started without testing compared to diuretic or renin-angiotensin-aldosterone system (RAAS) inhibitors.				
Monitoring and evaluation considerations	There is no guidance on how often these tests should be performed but analysis of the LIFE study showed regression/progression of ECG LVH or albuminuria was associated with improved/worse outcomes, independent of BP respectively.[25] [26]				
Research priorities	There needs to be greater understanding of the essential tests to be performed in all patients to reduce costs and improve outcomes.				