as the benefits observed with all therapies for PA are likely to outweigh the associated harms.

The panel also considered the economic implications of PA-specific therapies. While medical therapy has negligible costs, surgical treatment is associated with higher and variable costs depending on the country and health care system. Nonetheless, cost-effectiveness analyses generally favor PA-specific therapies. The panel concluded that the acceptability and feasibility of implementing these therapies depend on available resources and clinical expertise.

Given the overall certainty of the evidence regarding benefits and harms and recognizing that the implementation of PA-specific therapies varies by context, the panel issued a conditional recommendation for the use of PA-specific therapies over nonspecific antihypertensive treatments. This recommendation reflects the balance of evidence, contextual considerations, and resource variability across different settings.

The risk of MRA side effects can be minimized by commencing at low doses (eg, 12.5-25 mg of spironolactone daily) and increasing the dose gradually (eg, every 2-3 months or sooner if clinically indicated) as required to control BP (see Question 9. Table 10, Fig. 3).

Measurement of renin during MRA titration can assist in treatment decision making, but this is less straightforward if the individual is on other medications that affect renin levels (see Question 7).

Research Considerations

Current gaps in knowledge call for further research in the following areas:

- Assessing health equity after implementation of this recommendation
- Assessing efficacy and safety of newer nonsteroidal MRAs and aldosterone synthase inhibitors in the medical treatment of PA and developing new medications
- Conducting comparative effectiveness studies to assess PA-specific therapies (both medical and surgical) against nonspecific antihypertensive treatments in diverse clinical contexts and subgroups
- Studying the barriers to widespread adoption of PA-specific therapies, including clinician knowledge gaps, individual preferences, and logistical challenges associated with identifying lateralizing vs bilateral aldosterone production and treatment access
- Establishing large, diverse, and prospective cohorts to monitor long-term outcomes of PA-specific therapies, including cardiovascular and renal events, QOL, and cost-effectiveness
- Investigating disparities in access to PA-specific diagnostic and therapeutic interventions, particularly in low-resource settings and regions with limited access to AVS, surgical expertise, and newer medications

Screening for Primary Aldosteronism in Individuals With Hypertension

Background

Screening for primary aldosteronism (PA) allows for early identification and treatment, which can improve patient outcomes (Question 1). Several strategies exist for PA screening, with the most used approach being the measurement of aldosterone and renin (concentration or activity) and calculation of the aldosterone to renin ratio (ARR). This method may be more sensitive than relying solely on hypokalemia, as hypokalemia is present in only a minority of PA individuals (9%-37%), and many individuals with PA have normal potassium levels (90). Aldosterone and renin testing can identify normokalemic individuals with PA, expanding detection to a broader hypertensive population.

However, there are practical challenges to using aldosterone and renin for screening. The accuracy of these measurements can be influenced by medications, dietary sodium, and sampling conditions, which may lead to false positives or negatives. Additionally, the availability and cost of testing could limit the feasibility of widespread screening. In contrast, hypokalemia is simpler to detect, but screening for hypokalemia may miss many cases of PA, especially milder forms of the disease.

Given these considerations, the guideline evaluates whether measuring aldosterone and renin (including ARR) is a better strategy for screening for PA compared with relying on the detection of hypokalemia alone in individuals with hypertension.

Question 3. Should aldosterone (serum/plasma, or urine), renin (concentration or activity), and the aldosterone to renin ratio vs hypokalemia (unprovoked or diuretic-induced) be used for screening for primary aldosteronism in individuals with hypertension?

Recommendation 3

In individuals with hypertension, we suggest primary aldosteronism (PA) screening with serum/plasma aldosterone concentration and plasma renin (concentration or activity) (2 | ⊕⊕OO).

Technical remarks:

- Screen for PA by measuring serum/plasma aldosterone and plasma renin (concentration or activity) in the morning with individuals seated and avoiding dietary sodium restriction during the few days prior to screening. Potassium should be measured alongside renin and aldosterone— not for screening itself, but to aid in the accurate interpretation of aldosterone—as a low potassium may lead to a falsely low aldosterone.
- If screening results are negative and the patient has hypokalemia, potassium should be corrected to within the laboratory reference range and screening should be repeated.
- Manage interfering medications depending on individual safety and feasibility. The Guideline Development Panel (GDP) outlined both minimal-withdrawal and no-withdrawal strategies of interfering medications before screening (Tables 6 and 7, Fig. 1).
- A positive screen meets both of the following conditions in most circumstances:
  1. Renin is low/suppressed (hallmark of the diagnosis) and aldosterone is inappropriately high relative to renin: indicative of PA if plasma renin