Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease
rHuEPO therapy increases haemoglobin levels by at least 1gm/dl following every 4 weeks of treatment

Anemia improvement in patients with rHuEPO

Increment of Hb 2.0 g/dl compared to baseline
Increment of Hb 0.5 g/dl compared to baseline
Increment of Hb < 0.5 g/dl or any decrease of Hb level compared to baseline


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Within each recommendation, the strength of recommendation is indicated as Level 1 or Level 2, and the quality of the supporting evidence is shown as A, B, C, or D.

### NOMENCLATURE AND DESCRIPTION FOR RATING GUIDELINE RECOMMENDATIONS

**Reference keys**

**Level 1 ‘Strong’**

- "We recommend"
  - Most people in your situation would want the recommended course of action, and only a small proportion would not.

**Level 2 ‘Strong’**

- "We suggest"
  - The majority of people in your situation would want the recommended course of action, but many would not.

### Implications

<table>
<thead>
<tr>
<th>Grade</th>
<th>Quality of evidence</th>
<th>Patients</th>
<th>Clinicians</th>
<th>Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1 ‘Strong’</td>
<td>High</td>
<td>Most people in your situation would want the recommended course of action, and only a small proportion would not.</td>
<td>Most patients should receive the recommended course of action.</td>
<td>The recommendation can be evaluated as a candidate for developing a policy or a performance measure.</td>
</tr>
<tr>
<td>Level 2 ‘Strong’</td>
<td>Moderate</td>
<td>The majority of people in your situation would want the recommended course of action, but many would not.</td>
<td>Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.</td>
<td>The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.</td>
</tr>
</tbody>
</table>

### Grade Quality of evidence Meaning

<table>
<thead>
<tr>
<th>Grade</th>
<th>Quality of evidence</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>High</td>
<td>We are confident that the true effect is close to the estimate of the effect.</td>
</tr>
<tr>
<td>B</td>
<td>Moderate</td>
<td>The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.</td>
</tr>
<tr>
<td>C</td>
<td>Low</td>
<td>The true effect may be substantially different from the estimate of the effect.</td>
</tr>
<tr>
<td>D</td>
<td>Very low</td>
<td>The estimate of effect is very uncertain, and often it will be far from the true effect.</td>
</tr>
</tbody>
</table>

**CURRENT CHRONIC KIDNEY DISEASE (CKD) NOMENCLATURE USED BY KDIGO**

CKD is defined as abnormalities of kidney structure or function, present for > 3 months, with implications for health. CKD is classified based on Cause, GFR category (G1–G5), and Albuminuria category (A1-A3), abbreviated as CGA.

**Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012**

<table>
<thead>
<tr>
<th>Persistent albuminuria categories</th>
<th>Description and range</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>Normal to mildly increased</td>
</tr>
<tr>
<td>A2</td>
<td>Moderately increased</td>
</tr>
<tr>
<td>A3</td>
<td>Severely increased</td>
</tr>
<tr>
<td>Description and range</td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>Normal or high ≥ 90</td>
</tr>
<tr>
<td>G2</td>
<td>Mildly decreased 60–89</td>
</tr>
<tr>
<td>G3a</td>
<td>Mildly to moderately decreased 45–59</td>
</tr>
<tr>
<td>G3b</td>
<td>Moderately to severely decreased 30–44</td>
</tr>
<tr>
<td>G4</td>
<td>Severely decreased 15–29</td>
</tr>
<tr>
<td>G5</td>
<td>Kidney failure &lt; 15</td>
</tr>
</tbody>
</table>

**GREEN**, low risk (if no other markers of kidney disease, no CKD); **YELLOW**, moderately increased risk; **ORANGE**, high risk; **RED**, very high risk. GFR, glomerular filtration rate.
Summary of recommendation statements and practice points

The term “high BP” is used throughout the document to denote BP above the target for a particular population under consideration.

For most adult patients with CKD not receiving dialysis, the target is SBP <120 mm Hg (Chapter 3).

For adult kidney transplant recipients, the target remains SBP <130 mm Hg/DBP <80 mm Hg (Chapter 4).

For pediatric populations, mean arterial pressure (MAP) (calculated as DBP + 1/3 x pulse pressure) targets are age-dependent (Chapter 5).

Given that these targets vary according to the subpopulation of interest, we have avoided the term “hypertension” when referring to treatment decisions, as the term “hypertension” requires a single numerical definition and does not necessarily facilitate BP management.
Chapter 1. Blood pressure measurement

 Recommendation 1.1
 We recommend standardized office BP measurement in preference to routine office BP measurement for the management of high BP in adults (1B).

Practice Point 1.1: An oscillometric BP device may be preferable to a manual BP device for standardized office BP measurement; however, standardization emphasizes adequate preparations for BP measurement, not the type of equipment.

Practice Point 1.2: Automated office BP (AOBP), either attended or unattended, may be the preferred method of standardized office BP measurement.

Practice Point 1.3: Oscillometric devices can be used to measure BP among patients with atrial fibrillation.

 Recommendation 1.2
 We suggest that out-of-office BP measurements with ambulatory BP monitoring (ABPM) or home BP monitoring (HBPM) be used to complement standardized office BP readings for the management of high BP (2B).
Chapter 2. Lifestyle interventions for lowering blood pressure in patients with CKD not receiving dialysis

2.1. Sodium intake

- **Recommendation 2.1.1**
  We suggest targeting a sodium intake <2 g of sodium per day (or <90 mmol of sodium per day, or <5 g of sodium chloride per day) in patients with high BP and CKD (2C).

Practice Point 2.1.1: Dietary sodium restriction is usually not appropriate for patients with sodium-wasting nephropathy.

Practice Point 2.1.2: The Dietary Approaches to Stop Hypertension (DASH)–type diet or use of salt substitutes that are rich in potassium may not be appropriate for patients with advanced CKD or those with hyporeninemic hypoaldosteronism or other causes of impaired potassium excretion because of the potential for hyperkalemia.

2.2. Physical activity

- **Recommendation 2.2.1**
  We suggest that patients with high BP and CKD be advised to undertake moderate intensity physical activity for a cumulative duration of at least 150 minutes per week, or to a level compatible with their cardiovascular and physical tolerance (2C).

Practice Point 2.2.1: Consider the cardiorespiratory fitness status, physical limitations, cognitive function, and risk of falls when deciding on the implementation and intensity of physical activity interventions in individual patients.

Practice Point 2.2.2: The form and intensity of physical activity should be considered and modified as necessary in individual patients. There may still be important health benefits even if physical activity falls below targets proposed for the general population.
Chapter 3. Blood pressure management in patients with CKD, with or without diabetes, not receiving dialysis

3.1. Blood pressure targets

- **Recommendation 3.1.1**
  We suggest that adults with high BP and CKD be treated with a target systolic blood pressure (SBP) of <120 mm Hg, when tolerated, using standardized office BP measurement (2B).

Practice Point 3.1.1: It is potentially hazardous to apply the recommended SBP target of <120 mm Hg to BP measurements obtained in a non-standardized manner.

Practice Point 3.1.2: Clinicians can reasonably offer less intensive BP-lowering therapy in patients with very limited life expectancy or symptomatic postural hypotension.

3.2 Treatment with antihypertensive drugs, including RAS inhibitors (RASi)

- **Recommendation 3.2.1**
  We recommend starting renin-angiotensin-system inhibitors (RASi) (angiotensin-converting enzyme inhibitor [ACEi] or angiotensin II receptor blocker [ARB]) for people with high BP, CKD, and severely increased albuminuria (G1–G4, A3) without diabetes (1B).
Recommendation 3.2.2
We suggest starting RASi (ACEi or ARB) for people with high BP, CKD, and moderately increased albuminuria (G1–G4, A2) without diabetes (2C).

Recommendation 3.2.3
We recommend starting RASi (ACEi or ARB) for people with high BP, CKD, and moderately-to-severely increased albuminuria (G1–G4, A2 and A3) with diabetes (1B).

Practice Point 3.2.1: It may be reasonable to treat people with high BP, CKD, and no albuminuria, with or without diabetes, with RASi (ACEi or ARB).

Practice Point 3.2.2: RASi (ACEi or ARB) should be administered using the highest approved dose that is tolerated to achieve the benefits described because the proven benefits were achieved in trials using these doses.

Practice Point 3.2.3: Changes in BP, serum creatinine, and serum potassium should be checked within 2-4 weeks of initiation or increase in the dose of a RASi, depending on the current GFR and serum potassium.

Practice Point 3.2.4: Hyperkalemia associated with use of RASi can often be managed by measures to reduce the serum potassium levels rather than decreasing the dose or stopping RASi.

Practice Point 3.2.5: Continue ACEi or ARB therapy unless serum creatinine rises by more than 30% within 4 weeks following initiation of treatment or an increase in dose.
Practice Point 3.2.6: Consider reducing the dose or discontinuing ACEi or ARB in the setting of either symptomatic hypotension or uncontrolled hyperkalemia despite medical treatment, or to reduce uremic symptoms while treating kidney failure (estimated glomerular filtration rate [eGFR] <15 ml/min per 1.73 m²).

Practice Point 3.2.7: Mineralocorticoid receptor antagonists are effective for management of refractory hypertension but may cause hyperkalemia or a reversible decline in kidney function, particularly among patients with low eGFR.

3.3. Role of dual therapy with RASi

- **Recommendation 3.3.1**
  We recommend avoiding any combination of ACEi, ARB, and direct renin inhibitor (DRI) therapy in patients with CKD, with or without diabetes (1B).
Chapter 4. Blood pressure management in kidney transplant recipients (CKD G1T–G5T)

Recommendation 4.1
We recommend that a dihydropyridine calcium channel blocker (CCB) or an ARB be used as the first-line antihypertensive agent in adult kidney transplant recipients (1C).

Practice Point 4.1: Treat adult kidney transplant recipients with high BP to a target BP of <130 mm Hg systolic and <80 mm Hg diastolic using standardized office BP measurement (see Recommendation 1.1).

Chapter 5. Blood pressure management in children with CKD

Recommendation 5.1
We suggest that in children with CKD, 24-hour mean arterial pressure (MAP) by ABPM should be lowered to ≤50th percentile for age, sex, and height (2C).

Practice Point 5.1: We suggest monitoring BP once a year with ABPM, and monitoring every 3–6 months with standardized auscultatory office BP in children with CKD.

Practice Point 5.2: In children with high BP and CKD, when ABPM is not available, manual auscultatory office BP obtained in a protocol-driven standardized setting targeting achieved SBP <90th percentile for age, sex, and height of normal children is a reasonable approach.

Practice Point 5.3: Use ACEi or ARB as first-line therapy for high BP in children with CKD. These drugs lower proteinuria and are usually well tolerated, but they carry the risk of hyperkalemia and have adverse fetal risks for pregnant women.
In prophylaxis of organ rejection in patients receiving allogeneic renal, hepatic or cardiac transplants

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- Lower incidences of acute rejection in Tacrolimus plus Mycophenolate Mofetil (MMF)(TAC) group compared to Everolimus plus low - dose Cyclosporine (EVE) group (17% vs 23%, p=ns)¹

- Patients in EVE group showed higher serum cholesterol (205±41 vs. 235±41 mg/dL, p=0.0012) and lower hemoglobin concentration (13.6±1.4 vs. 12.4±1.9, p=0.01)¹

- Higher treatment discontinuation in the EVE group (MMF/TAC, 17% vs. EVE 36%, p=ns)¹

- Efficacy was similar in both EVE as well as (MMF) (TAC) groups¹

² In kidney transplantation patients, all subjects also received induction with basiliximab and corticosteroids.

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