The second study on the field was the African-American Study on Kidney Disease (AASK), a 3 × 2 factorial trial of 1094 African-Americans with hypertensive kidney disease [3, 4]. The mean baseline SBP was 149 mm Hg, MAP of 102–107 mm Hg or < 92 mm Hg, and to initial treatment with metoprolol, ramipril or amlopidine. The main outcomes were GFR slope and the composite of reduction in GFR by 50% or more (or ≥ 25 ml/min/1.73 m²), ESRD or death. The mean achieved SBP was 129/78 mm Hg (lower BP group 141/85 in the usual BP group. After a median follow-up of 3.8 years, neither the mean GFR slope (−2.21 ± 0.17 vs. −1.95 ± 0.17 ml/min/1.73 m² per year; P = 0.24) nor the composite outcome (risk reduction for intensive BP group 2%; 95% CI, 0.22% to 21%; P = 0.85) differed significantly between the BP groups whereas ramipril was associated with slower progression of renal disease [12].

After completing the trial phase of AASK, around 700 subjects were enrolled in a cohort phase in which the BP target was < 130/80 mm Hg, with total follow-up from 8.8 to 12.2 years. In the two phases together, there was no significant between-group difference in the risk of the composite outcome of doubling of serum creatinine (SCr), ESRD or death (HR in the intensive-control group, 0.91; 95% CI, 0.77–1.08). However, the outcome differed according to baseline proteinuria, as patients with urine-protein-to-creatinine ratio (UPCR) > 0.22 in 24-hour collections (roughly equivalent to 300 mg/day) had lower risk of the primary outcome with intensive treatment (HR 0.73; 95% CI, 0.57–0.93) whereas in those with UPCR ≤ 0.22 there was no difference between BP groups (HR, 1.18; 95% CI, 0.93–1.50) [13].

Taken together, the findings from MDRD and AASK indicate that a low BP target is beneficial for long-term renal survival in patients with non-diabetic proteinuric kidney disease. It must be noted, however, that all available evidence derives either from sub-group analyses or from combination of randomized phases with long-term observational phases of these trials, and still tentative evidence is available for this issue. Furthermore, trials randomized to MAP levels, which correspond on average, but not for every patient, to specific levels of systolic and diastolic BP. With that in mind, a goal BP of < 130/80 (i.e. that of the AASK cohort study) seems justifiable for patients with baseline proteinuria, as patients with urine-protein-to-creatinine ratio (UPCR) > 0.22 in 24-hour collections (roughly equivalent to 300 mg/day) had lower risk of the primary outcome with intensive treatment (HR 0.73; 95% CI, 0.57–0.93) whereas in those with UPCR ≤ 0.22 there was no difference between BP groups (HR, 1.18; 95% CI, 0.93–1.50) [13].

Blood pressure targets in non-diabetic kidney disease

The specific effects of different BP targets on hard renal end-points have been evaluated by two clinical trials in patients with non-diabetic CKD. The Modification of Diet in Renal Disease (MDRD) program included two sub-studies in patients with CKD of various aetiologies, of which 585 were in study A (a mean arterial pressure (MAP) < 107 mm Hg for patients ≤ 60 years (roughly corresponding to < 140/90 mm Hg) and < 113 mm Hg for patients > 60 years) or a low BP goal (MAP < 92 mm Hg for patients ≤ 60 years (corresponding to < 125/75 mm Hg) and < 98 mm Hg for patients > 61 years). The primary outcome was the rate of change in GFR (GFR slope) and the mean follow-up 2.2 years. Neither the projected decline in GFR (10.7 [95% CI, 9.1–12.4] vs. 11.5 [95% CI, 10.3–12.7] ml/min/1.73 m²) nor the risk of ESRD and death (0.85, 95% CI, 0.60–1.22 for the low BP group) differed significantly between the groups [8]. However, in detailed analyses dividing patients by baseline proteinuria, the low target BP was associated with a slower GFR decline in patients with urine protein excretion > 0.25 g/day in study A and > 1 g/day in study B [8, 9], even after adjustment for numerous covariates.

The above findings were confirmed in a patient-level meta-analysis of trials comparing the efficacy ACE-inhibitors in patients with predominantly non-diabetic CKD, showing that SBP levels of 110–119 and 120–129 mm Hg were associated with lower risk of kidney disease progression in patients with proteinuria > 1 g/day whereas in those with proteinuria < 1 g/day this association was not evident [10]. A subsequent analysis examined long-term outcomes of the MDRD study adding the trial phase (1989–1993) to a cohort period between 1993–2000, with a potential median follow-up of 10.7 years during which no specific target BP was recommended [11]. In the long run the low target BP was associated with a reduced risk of kidney failure (adjusted hazard ratio [HR] 0.68; 95% CI, 0.57–0.82) and composite outcome of ESRD or death (HR 0.77; 95% CI, 0.65–0.91), compared with the usual target BP. In subgroup analyses the benefits from low target BP were greater on SBP for ESRD and the composite end-point were again significant for patients with proteinuria > 1 g/day. These findings indicated that a low-target BP may be particularly beneficial in proteinuric patients and led to the recommendations for target BP described above.

**Table 1. Blood pressure targets for patients with CKD based on available evidence from renal and cardiovascular trials**

<table>
<thead>
<tr>
<th>Type of kidney disease</th>
<th>Protein excretion &lt; 0.3 g/day</th>
<th>Protein excretion 0.3–1 g/day</th>
<th>Protein excretion &gt; 1 g/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>(normalalbuminuria, microalbuminuria, 30–150 mg/day)</td>
<td>(microalbuminuria 150–300 mg/day, macroalbuminuria 300–500 mg/day)</td>
<td>(macroalbuminuria &gt; 500 mg/day)</td>
<td></td>
</tr>
<tr>
<td>Non-diabetic kidney disease</td>
<td>&lt; 140/90 mm Hg</td>
<td>&lt; 130/80 mm Hg</td>
<td>&lt;125/75 mm Hg*</td>
</tr>
<tr>
<td>Diabetic kidney disease</td>
<td>SBP &lt; 130–140 mm Hg**</td>
<td>&lt; 130/80 mm Hg</td>
<td>&lt;130/80 mm Hg***</td>
</tr>
<tr>
<td>DBP &lt; 80 mm Hg**</td>
<td>&lt; 125/75 mm Hg***</td>
<td>(for young patients with heavy proteinuria)</td>
<td></td>
</tr>
</tbody>
</table>

*As evident from MDRD study B trial phase and MDRD long-term study (see text); **from cardiovascular outcome trials (see text); ***through extrapolation from data in non-diabetic CKD and post-hoc or observational analyses in diabetic CKD (see text).
a 2.2-fold increase in the risk for doubling serum creatinine or ESRD compared with SBP < 134 mm Hg and follow-up achieved SBP most predicted re-
nal outcomes; moreover, progressive lowering of SBP to 120 mm Hg improved renal and patient survival, but below 120 mm Hg all-cause mortality increased. 

In conclusion, based on available data from observational analyses and surrogate outcomes and through extrapolation of evidence from non-diabetic proteinuric kidney disease, a BP < 130/80 mm Hg seems to protect kidney function in patients with diabetes and proteinuria and provides a better BP target derived from the UKPDS 38 study, which randomised 18,790 hypertensives to diastolic BP targets of 

References