KDIGO 2012 BP Guideline: Under Pressure

David C Wheeler

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KDIGO Controversies Conference
Blood Pressure Management in CKD

7th – 10th September 2017
Edinburgh, Scotland
Disclosures

• AstraZeneca
• Amgen
• Boehringer Ingleheim
• Janssen
• Merck
• Vifor Fresenius
Blood pressure in chronic kidney disease stage 5D—report from a Kidney Disease: Improving Global Outcomes controversies conference

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Kidney International (2010) 77, 273–284; doi:10.1038/kg.2009.469; published online 16 December 2009
2012 BP Guideline: Contributors

Guideline Co Chairs
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• David Wheeler (UK)

Work Group Non Diabetes
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• Cibele Rodrigues (Brazil)
• Hallvard Holdaas (Transplant) (Norway)

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• Sean Slifer

KDIGO Chairs
• Kai-Uwe Eckardt (Germany)
• Bertram Kasiske (USA)
2012 BP Guideline: Populations

- CKD Stages 1-5 not on dialysis
- Specific groups
  - Diabetes and Non-diabetes
  - Kidney transplant recipients
  - Children (<19)
  - Elderly
Interventions and Comparators

- Lifestyle modifications vs. placebo
- Blood pressure lowering agent vs. Placebo
- Drug Regimen A vs. Drug Regimen B
- Achieved target A/B vs. Achieved target C/D
Outcomes

- BP (lifestyle modifications only)
- Kidney – GFR, albuminuria, Dialysis
- Cardiovascular events
- Mortality
BP Guideline: Not in scope

- Patients receiving dialysis (stage 5D CKD)
- Prevention: patients with eGFR >60 ml/min/1.73m² without albuminuria*
- How to measure BP*
- Technical aspects of ambulatory BP monitoring or self measured BP*
- In depth pharmacological reviews*
- Management of renal artery stenosis*

*refer to prior guidelines as appropriate
BP Guideline Work Group Timetable

- Jan 16\textsuperscript{th} - 17\textsuperscript{th} 2010
  - Work Group Meeting 1
  - Boston

- May 8\textsuperscript{th} – 9\textsuperscript{th} 2010
  - Work Group Meeting 2
  - London

- Sep 11\textsuperscript{th}-12\textsuperscript{th} 2010
  - Work Group Meeting 3
  - New York

- Jan 2011
  - Draft Document

- July 2011
  - Publication date
KDIGO 2012 BP Guideline: Literature Yield

5885 total abstracts

130 abstracts selected after screening (based on eligibility - PICOT criteria)

62 abstracts
DKD

28 full-text articles accepted and extracted

57 abstracts
Non-DKD

33 full-text articles accepted and extracted

9 abstracts
Transplant

7 full-text articles accepted and extracted
KDIGO 2012 BP Guideline: Summary

- Lifestyle modifications as per no CKD
- \( \leq 140/90 \text{ mmHg} \)
- \( \leq 130/80 \text{ mmHg} \) if albuminuria (>3 mg/mmol)
- ACE or ARB if albuminuria (>3 mg/mmol)
- Individualize treatment

KDIGO Blood Pressure Work Group:
### KDIGO Blood Pressure Target: Recommendations in Stage 1-5 CKD

<table>
<thead>
<tr>
<th>Alb:Cr ratio mg/mmol</th>
<th>BP Target CKD No Diabetes</th>
<th>BP Target CKD with Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 (A1, normo)</td>
<td>≤ 140/90 (1B)</td>
<td>≤ 140/90 (1B)</td>
</tr>
<tr>
<td>3-30 (A2, micro)</td>
<td>≤ 130/80 (2D)</td>
<td>≤ 130/80 (2D)</td>
</tr>
<tr>
<td>&gt;30 (A3, macro)</td>
<td>≤ 130/80 (2C)</td>
<td>≤ 130/80 (2D)</td>
</tr>
</tbody>
</table>
# KDIGO blood pressure agents: Recommendations in stage 1-5 CKD

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<th>BP Target CKD No Diabetes</th>
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<tr>
<td>&lt;3 (A1, normo)</td>
<td>No recommendation</td>
<td>No recommendation</td>
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<tr>
<td>3-30 (A2, micro)</td>
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**KDIGO Blood Pressure Work Group:**
Controversies

- Should we maximise blockade of the renin-angiotensin system (aldosterone antagonists, direct renin inhibitors)?
- Should albuminuria reduction be a target for treatment with antihypertensive therapies?
- Should ACE and ARB be discontinued in stage 5 CKD because they compromise residual kidney function?
- Are there genetic/racial differences that need to be taken into account when treating blood pressure in CKD?
Future perspectives

- Renal data from ACCORD
- SPRINT trial
- Research recommendations
Three trials with a total of 2272 participants were included.

Lower blood pressure target of <130/80 mm Hg no more beneficial than a target of <140/90 mm Hg.

Participants in the low target groups had a slightly higher rate of adverse events.

Lower target may be beneficial in subgroups with proteinuria greater than 300 mg/d.

Kidney Disease: Improving Global Outcomes
Meta analysis: Subgroup analysis for kidney outcome by baseline proteinuria (0.3g/day)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Hazard Ratio (95% CI)</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
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<tbody>
<tr>
<td><strong>Patients without baseline proteinuria</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESCAPE 2009</td>
<td>0.75 (0.57, 1.00)</td>
<td>1.78 (0.62, 5.14)</td>
</tr>
<tr>
<td>MDRD 2010</td>
<td>1.39 (1.04, 1.86)</td>
<td></td>
</tr>
<tr>
<td>AASK 2010</td>
<td>0.75 (0.57, 1.00)</td>
<td>0.71 (0.59, 0.85)</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td>1.12 (0.66, 1.90)</td>
<td>0.71 (0.59, 0.85)</td>
</tr>
<tr>
<td>p=0.69 (I²=79.7%, p=0.007)</td>
<td></td>
<td>p&lt;0.001 (I²=18.5%, p=0.3)</td>
</tr>
<tr>
<td><strong>Patients with baseline proteinuria</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESCAPE 2009</td>
<td>0.53 (0.33, 0.87)</td>
<td></td>
</tr>
<tr>
<td>REIN-2 2005</td>
<td>1.00 (0.61, 1.64)</td>
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<tr>
<td>MDRD 2010</td>
<td>0.67 (0.53, 0.84)</td>
<td></td>
</tr>
<tr>
<td>AASK 2010</td>
<td>0.76 (0.58, 0.99)</td>
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<tr>
<td><strong>Overall</strong></td>
<td>0.76 (0.58, 0.99)</td>
<td>1.00 (0.61, 1.64)</td>
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<td>Lower target beneficial</td>
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Heterogeneity proteinuric vs. non proteinuric p=0.006

Mean achieved systolic blood pressures 131.7 vs. 141.5 mmHg

Lv et al, CMAJ, 2013;185:949-957
JNC8 committee recommendations

Recommendation 4
In the population aged ≥18 years with chronic kidney disease (CKD), initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to goal SBP <140 mm Hg and goal DBP <90 mm Hg. (Expert Opinion – Grade E)

Recommendation 8
In the population aged ≥18 years with CKD, initial (or add-on) antihypertensive treatment should include an ACEI or ARB to improve kidney outcomes. This applies to all CKD patients with hypertension regardless of race or diabetes status. (Moderate Recommendation – Grade B)

James PA et al, JAMA 2014;311:507-520
ACCORD study of BP targets in diabetes

**Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus**

The ACCORD Study Group

- **P** = 4733 patients with type 2 diabetes
- **I** = BP target <140 mmHg
- **C** = BP target <120 mmHg
- **O** = Cardiovascular events

**Kidney Events:**

- >1 x GFR < 30 ml/min/1.73m²
- Intensive therapy: 38%
- Standard therapy: 32% (p=0.46)

The ACCORD Study Group

NEJM 2010;362:1575-85
"US Officials said on 9th September that they decided to halt the study after an interim analysis of the data indicated that treating patients to achieve a target systolic BP of 120 mmHg instead of 140 mmHg cut the rate of cardiovascular events."

Lower Blood Pressure Guidelines Could Be ‘Lifesaving,’ Federal Study reveals

By GINA KOLATA SEPTEMBER 11, 2015
"Lowering of blood pressure into what has been regarded the normotensive range should therefore be routinely considered for the prevention of cardiovascular disease among those deemed to be of sufficient absolute risk".

New evidence that changes current KDIGO recommendations

David C Wheeler
University College London, UK
KDIGO Co Chair

American Society of Nephrology 2015
KDIGO 2012 BP Guideline: Reflection

- Recommendations divorced from evidence
- Unclear where data were extrapolated
- ± Diabetes does not really matter
- Pharmacopoeia unnecessary
- Implementation strategy?

KDIGO Blood Pressure Work Group:
Kidney Disease: Improving Global Outcomes

KDIGO 2017 Guideline Update