

KDIGO Clinical Guideline on Blood Pressure in CKD

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KDIGO Mission Statement

To improve the care and outcomes of kidney disease patients worldwide by promoting coordination, collaboration and integration of initiatives to develop and implement clinical practice guidelines.

KDIGO Guideline Process



“GRADE” system of grading of recommendations

Strength of Recommendation	1	Strong	Quality of evidence	A	High
	2	Weak or discretionary		B	Moderate
C				Low	
D	Very low				

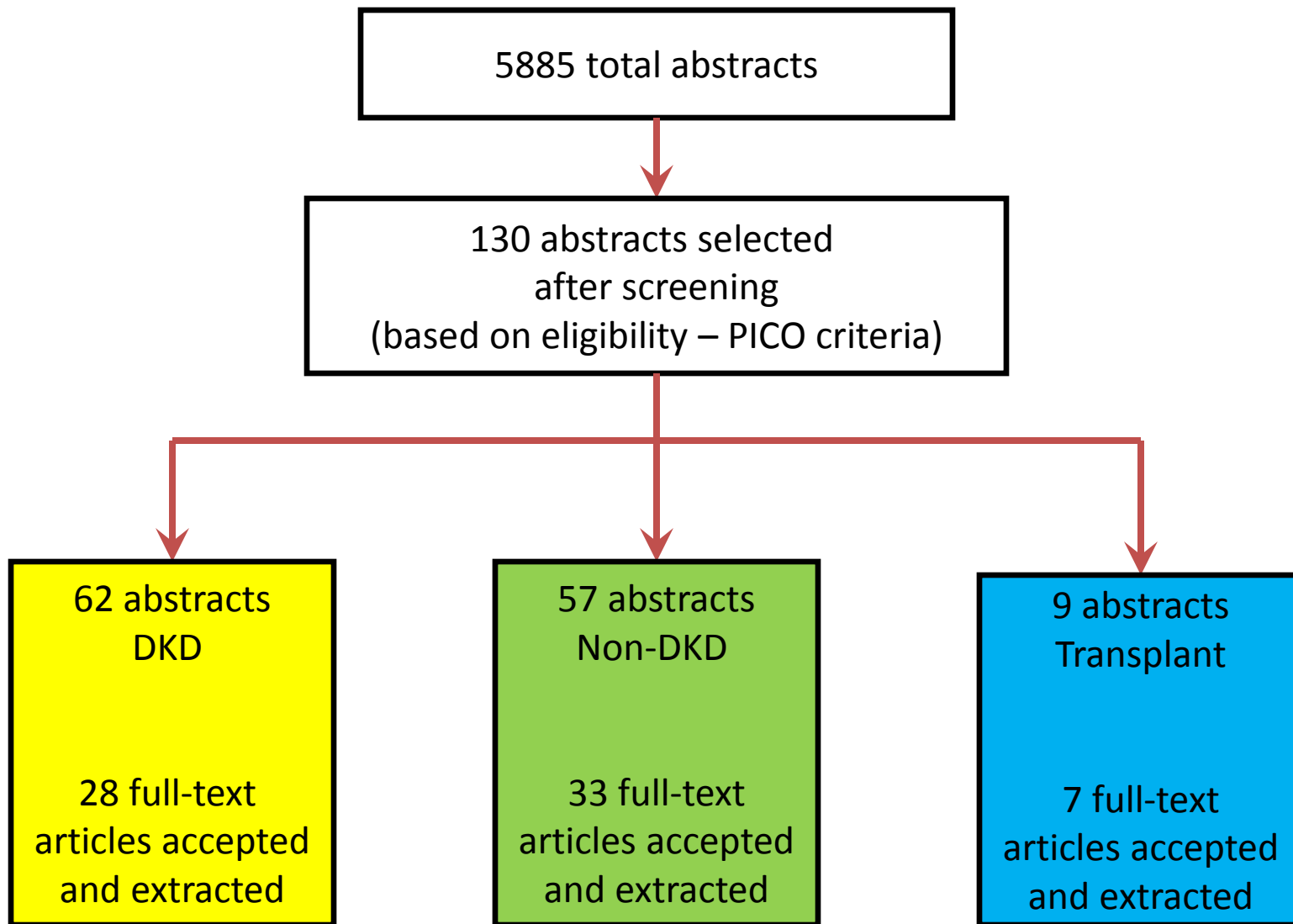
Options: 1A, 1B, 1C, 1D, 2A, 2B, 2D, 2D, or “not graded””

GENERAL STRATEGIES

2.1: Individualize BP targets and agents according to age, co-existent cardiovascular disease and other co-morbidities, risk of progression of CKD, presence or absence of retinopathy (in CKD patients with diabetes) and tolerance of treatment. (Not Graded)

2.2: Inquire about postural dizziness and check for postural hypotension regularly when treating CKD patients with BP-lowering drugs. (Not Graded)

Literature Yield

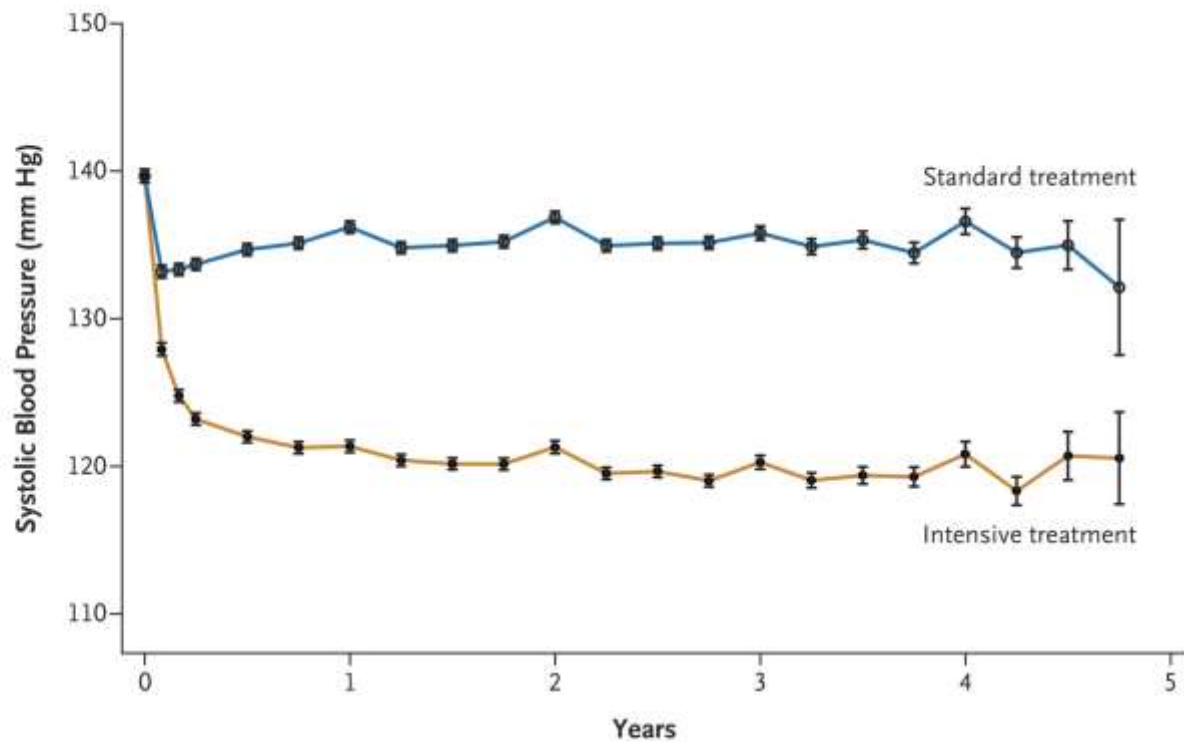


Our Scope

- BP targets for stages 1-5 CKD
- Not CKD 5D (dialysis)
- Lifestyle modifications that may lower BP
- Choice of antihypertensive agents
- Diabetes and no diabetes, Transplanted, Children (<19years) and Elderly (≥ 65 years)

Table S3. Causes of Death

Cause of death	Overall	Intensive	Standard
CVD Death	102	37	65
__ CHD Death	50	18	32
__ Stroke	17	8	9
__ Sudden cardiac death	13	2	11
__ CHF	17	8	9
__ Not cardiac but other cardiovascular	5	1	4
Non-CVD Death	192	90	102
__ Death from kidney disease	2	1	1
__ Death related to dialysis procedure	1	0	1
__ Other cardiac/non-ischemic	2	0	2
__ Cancer	101	49	52
__ Accident/Injury/Suicide/Homicide	14	4	10
__ Other noncardiac, nonstroke death	72	36	36
Undetermined	71	28	43
__ Unclassifiable	35	13	22
__ Not yet adjudicated	36	15	21
Total	365	155	210



No. with Data

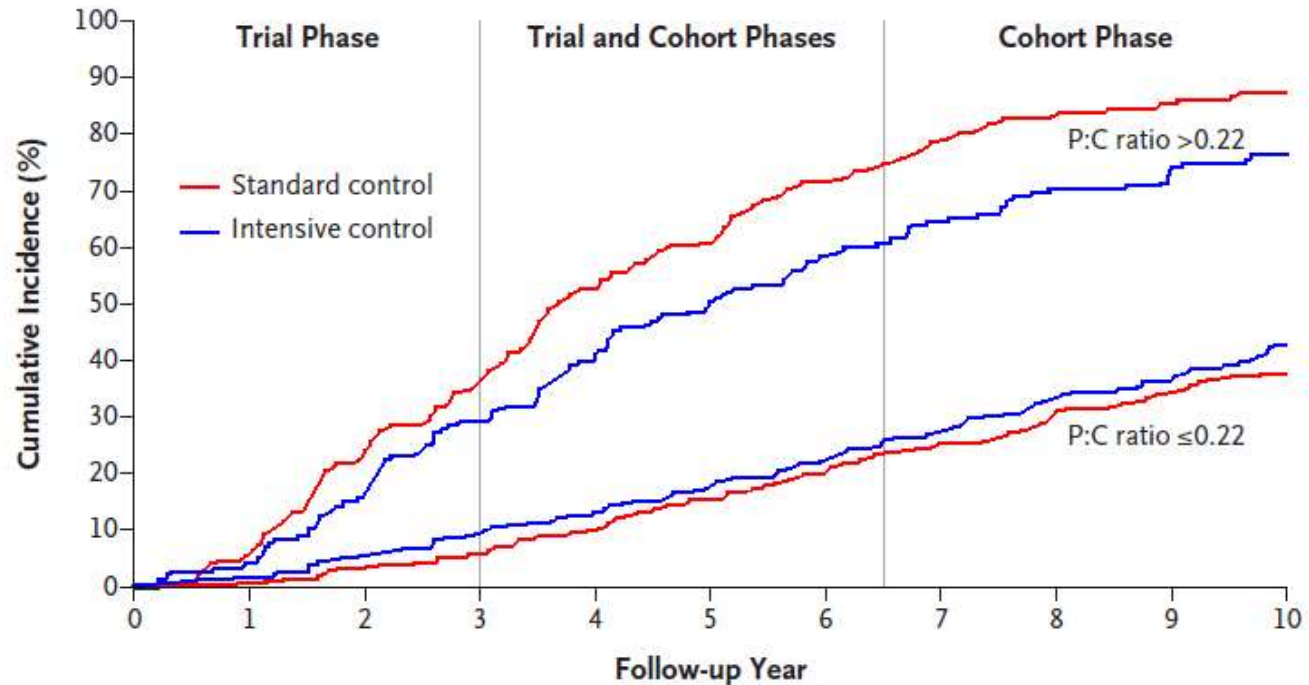
Standard treatment	4683	4345	4222	4092	3997	3904	3115	1974	1000	274
Intensive treatment	4678	4375	4231	4091	4029	3920	3204	2035	1048	286

Mean No. of Medications

Standard treatment	1.9	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9
Intensive treatment	2.3	2.7	2.8	2.8	2.8	2.8	2.8	2.8	2.8	3.0



AASK: Cumulative incidence of composite primary outcome



N=1094

P:C Ratio >0.22

Standard control	176	165	134	113	81	66	45	32	26	22	13
Intensive control	181	172	151	128	109	87	67	56	47	40	25

P:C Ratio ≤0.22

Standard control	376	373	362	353	332	302	267	234	214	196	128
Intensive control	357	350	335	321	306	282	254	228	206	189	128

Categories for Albuminuria

To allow assessment of RCTs where albuminuria or proteinuria was measured in different ways, and to enable recommendations based on these categories:

Albumin Excretion mg/day	ACR mg/mmol	PCR mg/mmol	Dipstick
<30	<3	<15	negative
30-300	3-30	15-49	1+
>300	>30	>50	2-3+

It is acknowledged that this brings approximations and inaccuracies depending on gender, age and other factors, but it is a pragmatic strategy.

Lifestyle and pharmacological treatments for lowering blood pressure in CKD ND patients

LIFESTYLE MODIFICATION

2.3: Encourage lifestyle modification in patients with CKD to lower BP and improve long-term cardiovascular and other outcomes:

2.3.1: We recommend achieving or maintaining a healthy weight (BMI 20 to 25). (1D)

2.3.2: We recommend lowering salt intake to ≤ 90 mmol (≤ 2 g) per day of sodium (corresponding to 5 g of sodium chloride), unless contraindicated. (1C)

2.3.3: We recommend undertaking an exercise program compatible with cardiovascular health and tolerance, aiming for at least 30 minutes 5 times per week. (1D)

2.3.4: We suggest limiting alcohol intake to no more than two standard drinks per day for men and no more than one standard drink per day for women. (2D)

Recommendations in CKD without diabetes mellitus

Albuminuria mg/day	BP Target mmHg	Preferred Agent
<30	<140/90 (1B)	None
30-300	<130/80 (2D)	ACEi or ARB (2D)
>300	<130/80 (2C)	ACEi or ARB (1B)

Chapter 3: BP management in CKD without diabetes

3.1: We recommend that non-diabetic adults with CKD and urine albumin excretion <30 mg/24 h (or equivalent*) whose office BP is consistently >140 mm Hg during systole or >90 mm Hg during diastole be treated with BP-lowering drugs to maintain a BP that is consistently ≤ 140 mm Hg systolic and ≤ 90 mm Hg diastolic. (1B)

*Approximate equivalents for albumin excretion per day in terms of dipstick, albumin/creatinine ratio, albumin excretion per minute, protein excretion per day and protein/creatinine ratio are given (table).

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Total	365	155	210

3.1: We recommend that non-diabetic adults with CKD ND and urine albumin excretion ≥ 30 mg per 24 hours (or equivalent*) whose office BP is consistently ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤ 140 mm Hg systolic and ≤ 90 mm Hg diastolic. (1B)

3.2: We suggest that non-diabetic adults with CKD ND and urine albumin excretion of 30 to 300 mg per 24 hours (or equivalent*) whose office BP is consistently ≥ 130 mm Hg systolic or ≥ 80 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤ 130 mm Hg systolic and ≤ 80 mm Hg diastolic. (2D)

3.3: We suggest that non-diabetic adults with CKD ND and urine albumin excretion ≥ 300 mg per 24 hours (or equivalent*) whose office BP is consistently ≥ 130 mm Hg systolic or ≥ 80 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently < 130 mm Hg systolic and < 80 mm Hg diastolic. (2C)

3.4: We suggest that an ARB or ACE-I be used in non-diabetic adults with CKD ND and urine albumin excretion of 30 to 300 mg per 24 hours (or equivalent*) in whom treatment with BP-lowering drugs is indicated. (2D)

3.5: We recommend that an ARB or ACE-I be used in non-diabetic adults with CKD ND and urine albumin excretion ≥ 300 mg per 24 hours (or equivalent*) in whom treatment with BP-lowering drugs is indicated. (1B)

Blood pressure management in CKD ND patients with diabetes mellitus

Recommendations in CKD with diabetes mellitus

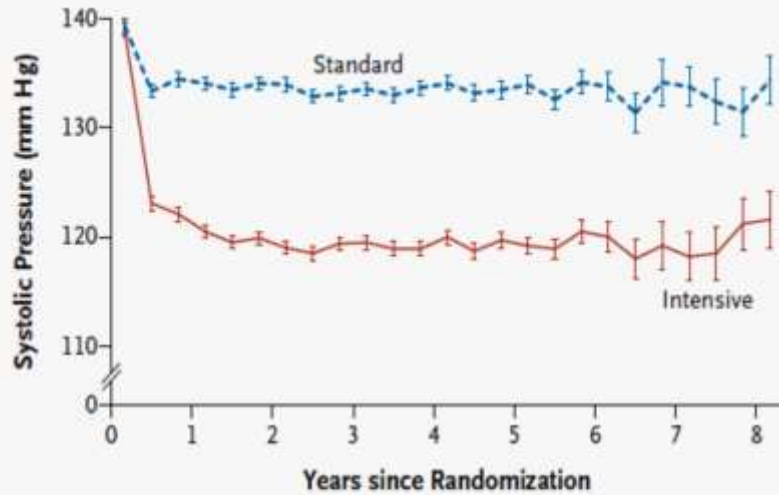
Albuminuria mg/day	BP Target mmHg	Preferred Agent
<30	<140/90 (1B)	None
30-300	<130/80 (2D)	ACEi or ARB (2D)
>300	<130/80 (2D)	ACEi or ARB (1B)

ACCORD BP

- 4733 Type 2 DM, with vascular disease (40 yr), or risk (≥ 55 yr), <80 yr.
- Cr not >1.5 mg/dL, proteinuria <1 g/day.
- RCT SBP <140 mmHg or <120 mmHg
- Also RCT of control of glucose and other factors

Cushman et al NEJM 2010; 362; 1575-1585

ACCORD



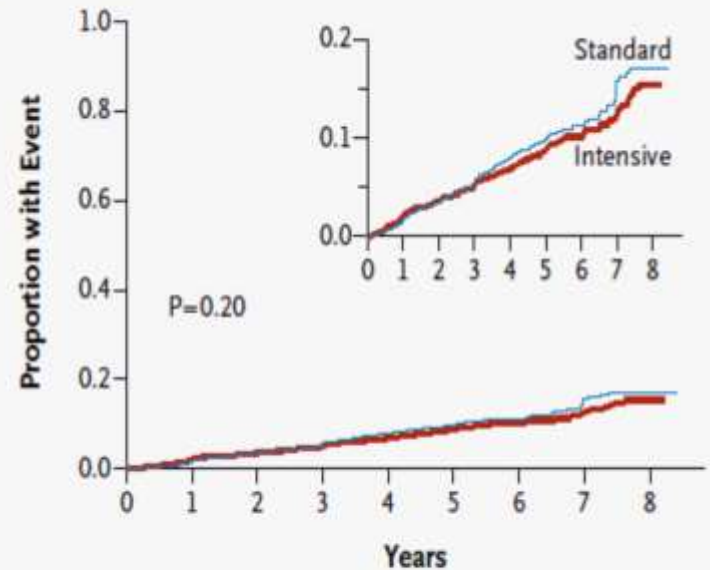
Mean No. of Medications Prescribed

Intensive	3.2	3.4	3.4	3.5	3.5	3.5	3.4	3.4
Standard	1.9	2.1	2.1	2.2	2.2	2.3	2.3	2.3

No. of Patients

Intensive	2174	2071	1973	1792	1150	445	156	156
Standard	2208	2136	2077	1860	1241	504	203	201

A Primary Outcome



No. at Risk

Intensive	2362	2273	2182	2117	1770	1080	298	175	80
Standard	2371	2274	2196	2120	1793	1127	358	195	108

4.1: We recommend that adults with diabetes and CKD ND with urine albumin excretion ≥ 30 mg per 24 hours (or equivalent*) whose office BP is consistently ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤ 140 mm Hg systolic and ≤ 90 mm Hg diastolic. (1B)

4.2: We suggest that adults with diabetes and CKD ND with urine albumin excretion ≥ 30 mg per 24 hours (or equivalent*) whose office BP is consistently ≥ 130 mm Hg systolic or ≥ 80 mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤ 130 mm Hg systolic and ≤ 80 mm Hg diastolic. (2D)

4.3: We suggest that an ARB or ACE-I be used in adults with diabetes and CKD ND with urine albumin excretion of 30 to 300 mg per 24 hours (or equivalent*). (2D)

4.4: We recommend that an ARB or ACE-I be used in adults with diabetes and CKD ND with urine albumin excretion 4300 mg per 24 hours (or equivalent*). (1B)

**Blood pressure management in
kidney transplant recipients
(CKD T)**

Chapter 7: Kidney transplant recipients

6.1: We suggest that in adult kidney transplant recipients whose office blood pressure is consistently >130 systolic and/or >80 diastolic be treated with blood pressure lowering drugs to maintain systolic BP consistently ≤ 130 and diastolic consistently ≤ 80 , irrespective of level of albuminuria. *(2D)*

6.2: It is reasonable that in adult kidney transplant recipients, choice of blood pressure lowering agent be influenced by time after transplant, use of CNI's, presence of persistent proteinuria and comorbid conditions. *(Not Graded)*

Children – ESCAPE TRIAL

- 3-18 years, N = 385
- All on ramipril
- 24hr Ambulatory BP: 50th percentile (Intensive BP control) vs. 50-95 percentile (Conventional BP control)
- 5 year follow-up
- Primary end points ESKD or 50% reduction in GFR
- Secondary end points BP, GFR, Urinary protein.

Chapter 8: Children with CKD

6.1: We recommend that in children with CKD, blood pressure lowering treatment is started when the blood pressure is above the 90% percentile for age/gender/height. *(1B)*

6.2: We suggest that in children with CKD with pretreatment blood pressure above the 90% percentile for age/sex/height, blood pressure is lowered to below the 50th percentile for age/sex/height. *(2C)*

6.3: It is reasonable that in children with CKD choice of blood pressure agent be influenced by age, cause of CKD and comorbid conditions. *(Not Graded)*

5.1: We suggest that adult kidney transplant recipients whose office BP is consistently ≥ 130 mm Hg systolic or ≥ 80 mm Hg diastolic be treated to maintain a BP that is consistently < 130 mm Hg systolic and < 80 mm Hg diastolic, irrespective of the level of urine albumin excretion. (2D)

5.2: In adult kidney transplant recipients, choose a BP-lowering agent after taking into account the time after transplantation, use of calcineurin inhibitors, presence or absence of persistent albuminuria, and other co-morbid conditions. (Not Graded)

Blood pressure management in elderly persons with CKD ND

Chapter 9: The elderly with CKD

9.1: It is advisable to tailor treatment regimens closely to co-morbidities and their therapies, with very gradual escalation of treatment, and close attention to potential adverse events related to BP treatment including electrolyte disorders, acute deterioration in renal function and orthostatic hypotension. (*Not Graded*)

7.1: Tailor BP treatment regimens in elderly patients with CKD ND by carefully considering age, co-morbidities and other therapies, with gradual escalation of treatment and close attention to adverse events related to BP treatment, including electrolyte disorders, acute deterioration in kidney function, orthostatic hypotension and drug side effects. (Not Graded)

The whole guideline in one slide

- Target <140/90 mmHg for CKD patients without albuminuria
- Lower target (<130/80 mmHg) if (any) albuminuria
- Consider lifestyle changes
- ACE/ARB preferred if ACR >30 mg/24hr (whether or not diabetes is present)
- Lower target (<130/80mmHg) in transplant recipients
- Tailor treatment depending on co-morbidities
- Take care in the elderly

Least popular recommendation

Recommendation 4.4: We suggest that an ARB or ACE inhibitor be used as first-line therapy in adult with CKD-ND and diabetes (with urine albumin excretion >30 mg/24 h or equivalent) in whom treatment with BP-lowering drugs is otherwise not indicated (i.e. Without hypertension). (2D)

ACCEPTABLE		134	93%	
UNACCEPTABLE		10	7%	
		Total	144	100%

Controversies

- 8.1 How should blood pressure be measured?
- 8.2 Is there evidence for a lower limit BP target level?
- 8.3 Should albuminuria reduction be a target for treatment with antihypertensive therapies?
- 8.4 Should we maximise blockade of the renin- angiotensin system (aldosterone antagonists, direct renin inhibitors)?
- 8.5 Should ACE and ARB be discontinued in stage 5 CKD because they compromise residual kidney function?
- 8.6 Should ethnicity, race and genes influence treatment?

KDIGO BP Guideline: Headlines

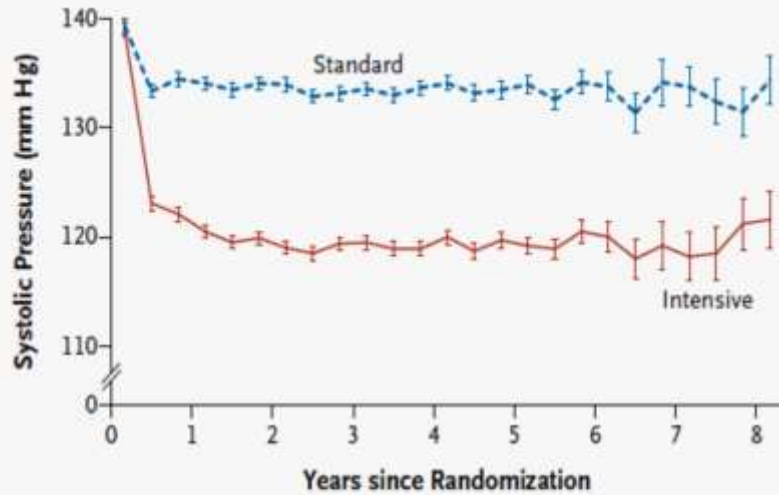
- Target BP = Threshold for treatment
- Individualize treatment
- Balance risk vs. benefit
- Graded approach including lifestyle
- Action depends on +/- albuminuria
- ACE/ARB preferred in specific group
- Cautious approach in the elderly

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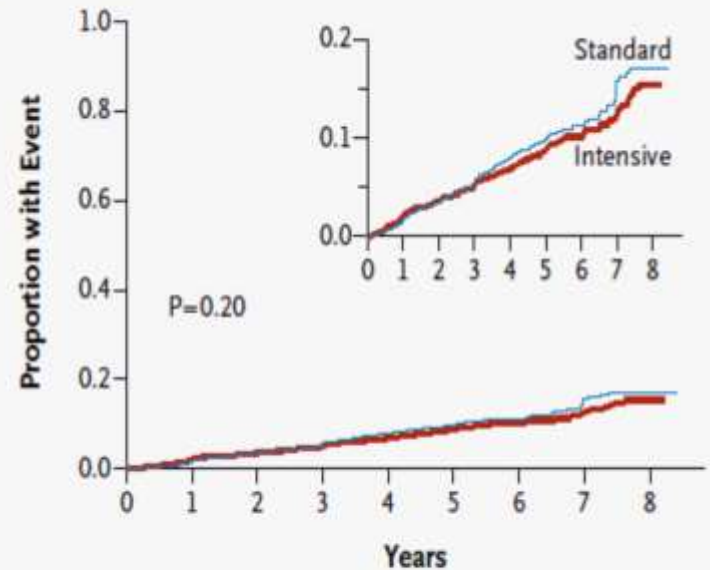
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