ABCD and Renal Association Clinical Guidelines for Diabetic Nephropathy-CKD. Management of Dyslipidaemia and Hypertension in Adults

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Rationale

- No national practical evidence based guidelines for holistic management of diabetic nephropathy and CKD through the spectrum in type 1 and type 2 diabetes
- Recognition that diabetes and renal physicians need to apply a mutually agreed set of principles which benefits from pooled expertise and experience

Process

- Working party and writing group set up initially in 2013
- Formal writing group work programme from 2014-2106
- Use of RA Clinical Guidelines criteria for grading evidence based recommendations
- Pubmed , MEDLINE and Cochrane database were searched for relevant papers and all relevant national and international guidelines reviewed

The team !

Management of lipid abnormalities in adults with DM and nephropathy-CKD

- Lipid metabolism differs in type 1 V type 2 DM
- T1DM - HDLC high unless severe insulin deficiency
- T2DM insulin resistance - dyslipidaemic picture (raised Trigs and reduced HDLC) .
- Progressive CKD reduces HDL , Progressive proteinuria increases LDL
- Compositional atherogenic abnormalities seen with renal dysfunction in both T1 and T2 DM

Recommendations for statins in T1DM

- All aged 40+ with normal renal function unless new LADA in well controlled DM with high HDLC
- All aged > 30 with persistent raised ACR
- Progressive early CKD (eGFR fall > 5 ml/min/yr)
- All with CKD3 or worse
- Aged 18-30 with persistent albuminuria especially with other CVD risk factors

Recommendations for statins in T2DM

- All patients with CKD1-2 with albuminuria irrespective of age
- All patients with CKD3 or worse regardless of age
- Continue statins if dialysis commenced
- Commence statins in those starting dialysis especially if younger patients
- Commence-continue statins after renal transplantation

Statin dosage

- Atorvastatin 20 mg - If simvastain used, never more than 40 mg (20 mg Simvastatin is maximum dose if on Calcium Antagonist)
- High intensity 40-80 mg Atorvastatin if target TC 4 or non HDL C 2.5 not attained (especially in higher CVD risk with HbA1c > 75 , smoking , dyslipidaemia , HBP , PDR)
- High intensity in all with CVD

Statin intolerance

- Submaximal dose , rechallenge , switch statin
- Ezetimibe add on
- PCSK9 Inhibitors – no current data or indication
- No role for fibrates in advanced CKD 3B-5
- Fenofibrate alone or with statin only in DM CKD3A or earlier stages to reduce microvascular events in those with residual dyslipidaemia
- Fenofibrate monitor eGFR – no role in combination with ezetimibe

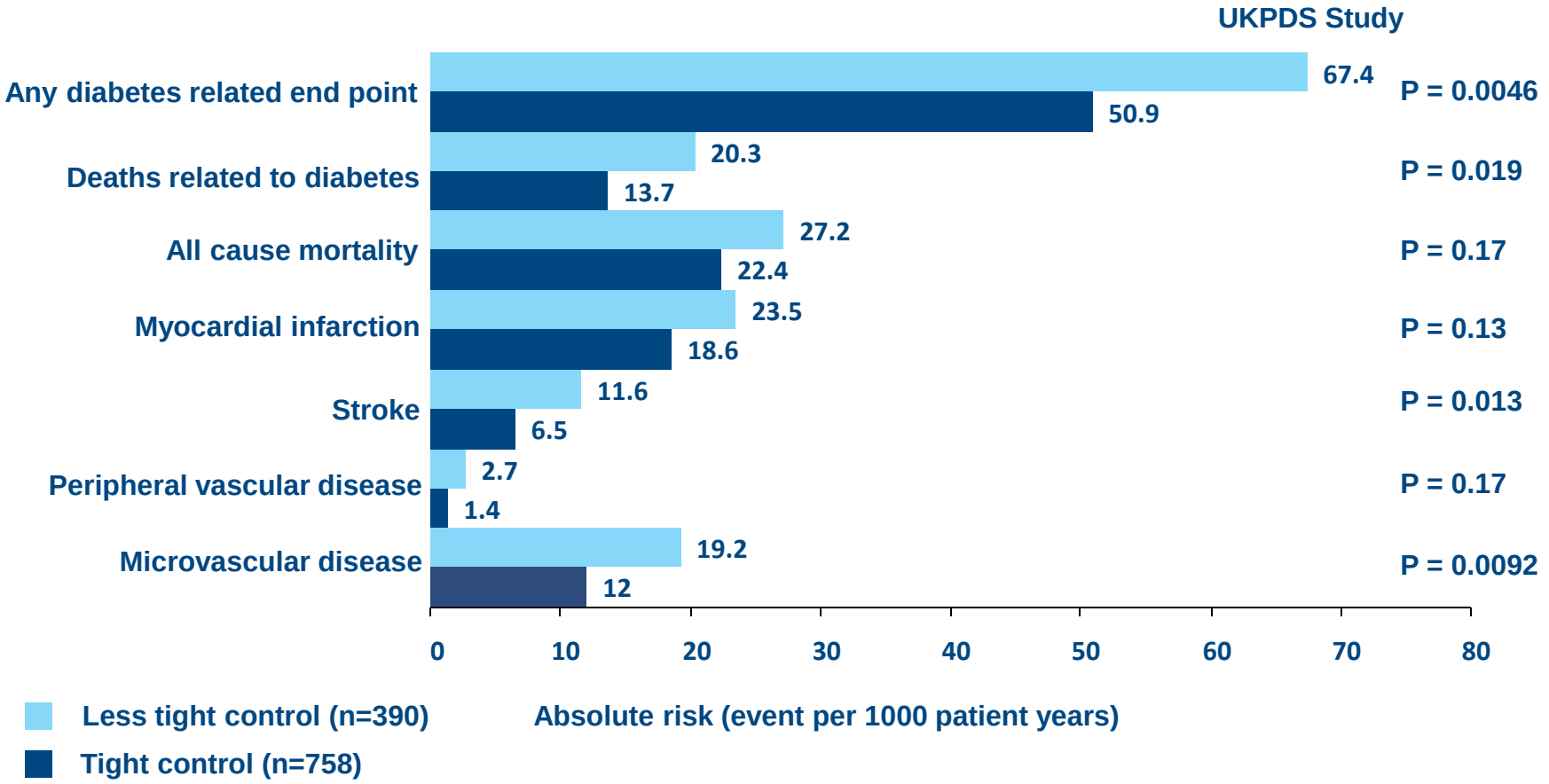
Audit standards

- Proportion of patients with T1 and T2 DM at separate CKD-DM stages on statins
- Proportion of patients in these categories achieving key non HDLC target of < 2.5 mmol/l
- Use of non statin therapies (e.g ezetimibe and fenofibrate)

Areas for further research

- Statins impact on renal function – limited benefit short term on proteinuria , none on GFR
- Role of PCSK9 Inhibitors in DM DN-CKD with or without CVD

BP control in diabetes reduces complications

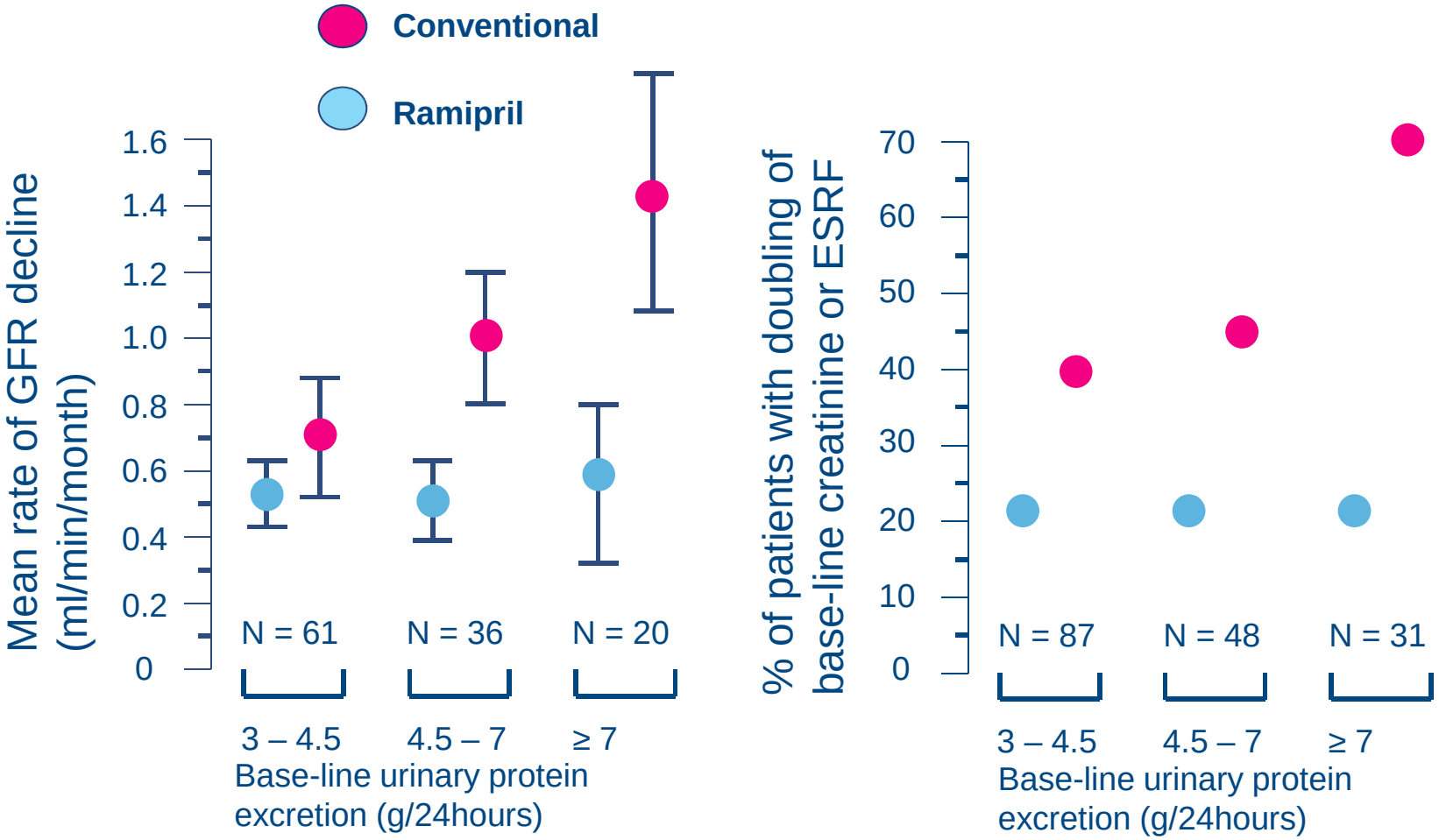


Mean BP <180/100 vs <150/85 mmHg

UK Prospective Diabetes Study (UKPDS) Group. *BMJ* 1998; 317: 703–713

ACEi decrease proteinuria and slow progression

REIN Study

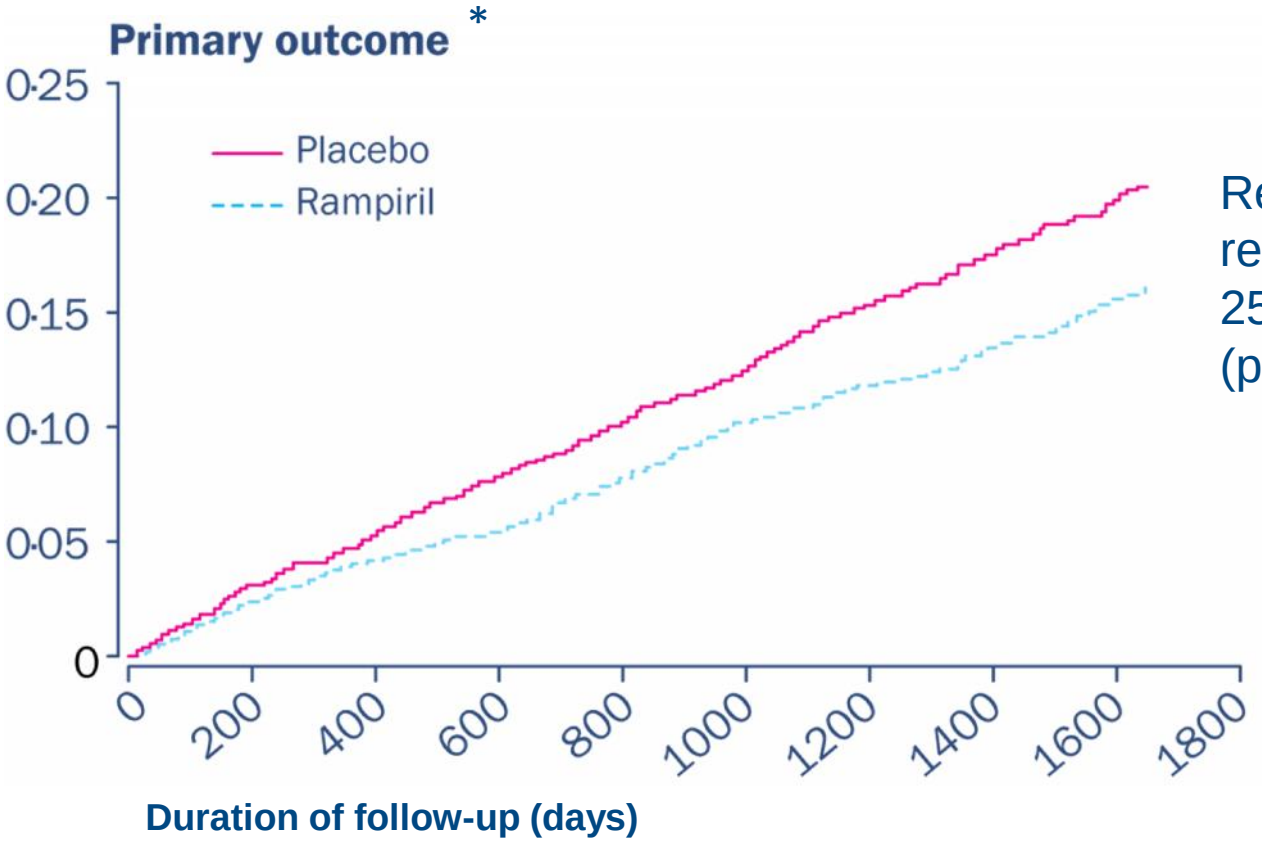


Adapted from GISEN Study Group. *Lancet* (1997) 349: 1857-1863

ACE-inhibitor control of blood pressure

*myocardial infarction, stroke, or CV death

HOPE Study



Relative risk reduction 25% (p=0·0004)

Adapted from HC Gerstein, *Lancet* 2000; 355: 253–59

ABCD RA Guideline for management of hypertension in diabetic nephropathy-chronic kidney disease

- Management of hypertension in patients with type 1 diabetes (T1D) and nephropathy
- Management of hypertension in patients with type 2 diabetes (T2D) and early CKD (stages 1 and 2)
- Management of hypertension in patients with diabetes and CKD stages 3, 4 and 5ND
- Management of hypertension in patients with diabetes who are on dialysis (CKD 5D)

Recommendations – T1D

- In patients with T1D and normoalbuminuria, we recommend a threshold for BP therapy ≥ 140/80 mmHg (Grade 1B).
- In T1D and persistent micro- or macro-albuminuria, we recommend that ACEI therapy should be considered irrespective of BP , and that the target upright BP should be ≤130/80 mmHg. (Grade 1B).
- There is no current evidence to support a role for ACEI therapy for BP or renal protection in normotensive, normoalbuminuric patients with T1D (Grade 1C).
- There is no firm evidence to support a role of dual RAAS blockade in patients with T1D (Grade 1C).

Research recommendations – T1D

- Presence of microalbuminuria may not be the best predictor of progressive CKD. What is the role for other markers (e.g. KIM-1)?
- What is the role of dual blockade in T1D nephropathy?
- What is the role of aldosterone receptor blockers or direct renin inhibitors in patients with T1D and nephropathy?
- Is there a role for home or ABP monitoring in the diagnosis and management of hypertension in T1D, particularly in those with autonomic neuropathy?
- What is the role of RAAS-blocking agents in patients with T1D, progressive renal decline and normoalbuminuria?

Recommendations for T2D with early CKD

- In patients with T2D and hypertension, we recommend salt intake of <5 g/d NaCl (Grade 1C).
- In patients T2D, CKD and ACR<3 mg/mmol, we recommend target BP of <140/90 mmHg (Grade 1D).
- In patients with T2D, CKD and ACR >3 mg/mmol, we suggest a target BP of <130/80 mmHg (Grade 2D).
- We recommend that ACEIs (or ARBs if ACEI not tolerated) should be used in patients with T2D and CKD who have ACR >3 mg/mmol (Grade 2D). No evidence for dual RAAS blockade.
- There is no evidence to support ACEI or ARB as first-line agent for T2D, normal renal function and normal UAE (Grade 1A).

Recommendation for DM CKD stages 3-5

- We recommend monitoring of BP, ACR and U&E 2 to 4 times per year, depending on the stage of CKD and patient's need (Grade 1B).
- We recommend initiation of antihypertensive agents in patients with DM CKD 3-5 and ACR of <30 mg/mmol when their BP is >140/90 mmHg and a target of ≤140/90 mmHg (Grade 1B).
- We suggest initiation of antihypertensive agents in patients with DM CKD 3-5 and an ACR >30 mg/mmol when their BP >130/80 mmHg, and a target BP ≤130/80 mmHg (Grade 2C).
- We recommend the use of an ACEI (or an ARB if ACEI is not tolerated) as the first choice BP lowering agent in patients with DM CKD 3-5 and micro and macro-albuminuria (Grade 1B).

Research recommendations DM CKD 3-5

- What is the effect of intensive BP lowering (≤130/80 mmHg) on renal and cardiac outcomes in patients with DM CKD 3-5?
- What is the impact of dual RAAS blockade on renal and cardiac outcomes in patients with diabetes, CKD and proteinuria?
- What is the impact of aldosterone blockade on renal and cardiac outcomes in patients with DM CKD?
- What is the effect of long-term use of novel potassium binders together with RAAS blockade on renal and cardiac outcomes in patients with DM CKD?

Recommendations for DM CKD 5D

- We recommend that ABP or HBP measurement should be used to monitor BP in patients with DM CKD 5D (Grade 1C).
- Where ABP or HBP are not feasible, we suggest using pre, intra and post-dialysis BP measurements for HD patients, and clinic BP for PD patients(Grade 2D).
- We recommend volume control as a first-line management to optimise BP control (Grade 1B).
- We suggest salt reduction to less than 5 g/day to optimise blood pressure control (Grade 2C).
- We suggest a target upright inter-dialytic BP of ≤140/90 for patients with DM CKD 5D. Individualisation of the BP target for older patients with multiple comorbidities, to reduce adverse effects of BP lowering (Grade 2D).

Research recommendation DM CKD 5D

- Which BP measurement should be used to reduce LVH and mortality: pre-dialysis, post-dialysis, home or ABP?
- What is the optimal BP target?
- Does treatment with ACEI, ARB, calcium channel blockers or beta-blockers to lower BP reduce CV morbidity and mortality?
- Does salt restriction (<5 g/d) in patients with diabetes who are on dialysis influence BP control or CV outcomes?
- Is there a role for diuretic therapy in patients with diabetes who are on dialysis and have residual renal function?

Conclusion - BP guideline

- BP control and RAAS blockade are important in patients with diabetes and CKD
- However, there is lack of high quality evidence
- Most of the recommendations are based on moderate to very low quality evidence or extrapolation from evidence in non-diabetes CKD
- Particularly true for patients with diabetes who are on dialysis
- Therefore, a number of research recommendations have been made
- Further research to inform future guidelines