



Case Discussions: How to Manage Diabetic Nephropathy, Part 1

January 23, 2026 | Brendan McCormick

PRESENTER DISCLOSURE

- **Presenter:** Brendan McCormick
- **Relationships with commercial interests:**
 - **Grants/Research Support:** None
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 - **Consulting Fees:** None

LEARNING OBJECTIVES

1. The diagnosis and natural history of diabetic kidney disease
2. The role of angiotensin receptor blockers and ACE-inhibitors in diabetic kidney disease
3. How to monitoring of patients on RAS blockade

Case for Discussion

- 48 year old male new to your practice
 - History of hypertension treated with indapamide 2.5 mg daily, otherwise healthy, non smoker
 - Family history of diabetes
 - On exam obese, BMI 35, BP 120/80
 - UA 2+ protein, no blood, ACR 42 mg/mmol, Cr 62umol/L, K 3.6 mmol/L, FBG 9 mmol/L, HBA1C 7.1%

Question 1

- Does this patient have diabetic nephropathy:
 1. Yes
 2. No
 3. Needs more tests

Ontario Renal Network

IDENTIFY high-risk CKD populations

- Hypertension (HTN)
- Diabetes mellitus
- Cardiovascular disease
- First degree relative with CKD
- First Nations, Inuit, Métis, or urban Indigenous people(s)



MEASURE eGFR and urine ACR

- If eGFR < 60, re-measure in 3 months, or sooner if clinical concern dictates (rapid decline or very low)
 - If urine ACR ≥ 3 , re-measure 1 or 2 times over next 3 months (abnormal result: at least 2 of 3 results ≥ 3)
- CKD detection should be done in the absence of acute intercurrent illness or self-limited illness. Consider reversible causes prior to re-measuring (e.g. NSAIDs, contrast diagnostic imaging dye, BPH/urinary retention).

For more information on KidneyWise, visit **KidneyWise.ca**

For information on the Kidney Failure Risk Equation visit **ontariorenalnetwork.ca/en/kidney-care-resources/clinical-tools/primary-care/kfre**

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CONFIRM CKD diagnosis after 3 months

**eGFR < 30 and/or ACR > 60
Person has CKD**

Check electrolytes and urine R+M
Check CBC, Calcium, Phosphate, Albumin

Refer to nephrology
with co-morbid conditions and lab values with trends of urine ACR, eGFR, and BPs
Cardiovascular disease
First degree relative of CKD

**eGFR 30–59 and/or ACR 3–60
Person has CKD**

Monitor in Primary Care
Check electrolytes and urine R+M
Follow eGFR & urine ACR every 6 months

- If eGFR remains stable for 2 years, follow both measures yearly
- **FLAG:** If any of the following, refer to nephrology with co-morbid conditions and lab values with trends of urine ACR, eGFR, BPs
 - › eGFR < 30 or ACR > 60
 - › eGFR < 45 and rapid decline of > 5 ml/min within 6 months, repeated in 2-4 weeks
 - › 5-year Kidney Failure Risk Equation $\geq 5\%$
 - › Inability to achieve BP targets
 - › Significant electrolyte disorder
 - › RBC casts or hematuria (> 20 RBC/hpf) suggestive of GN/renal vasculitis

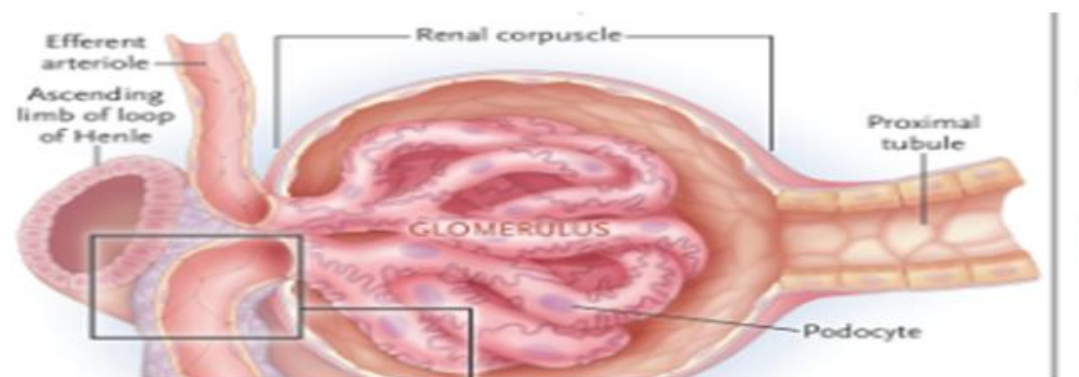
**eGFR ≥ 60 and ACR < 3
Person does not have CKD**

Re-measure annually for people with diabetes mellitus
Otherwise, re-measure less frequently unless clinical circumstances dictates

For more information on KidneyWise, visit [KidneyWise.ca](https://www.kidneywise.ca)

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Random Urine Albumin Measurements



ALBUMINURIA CATEGORIES IN CKD

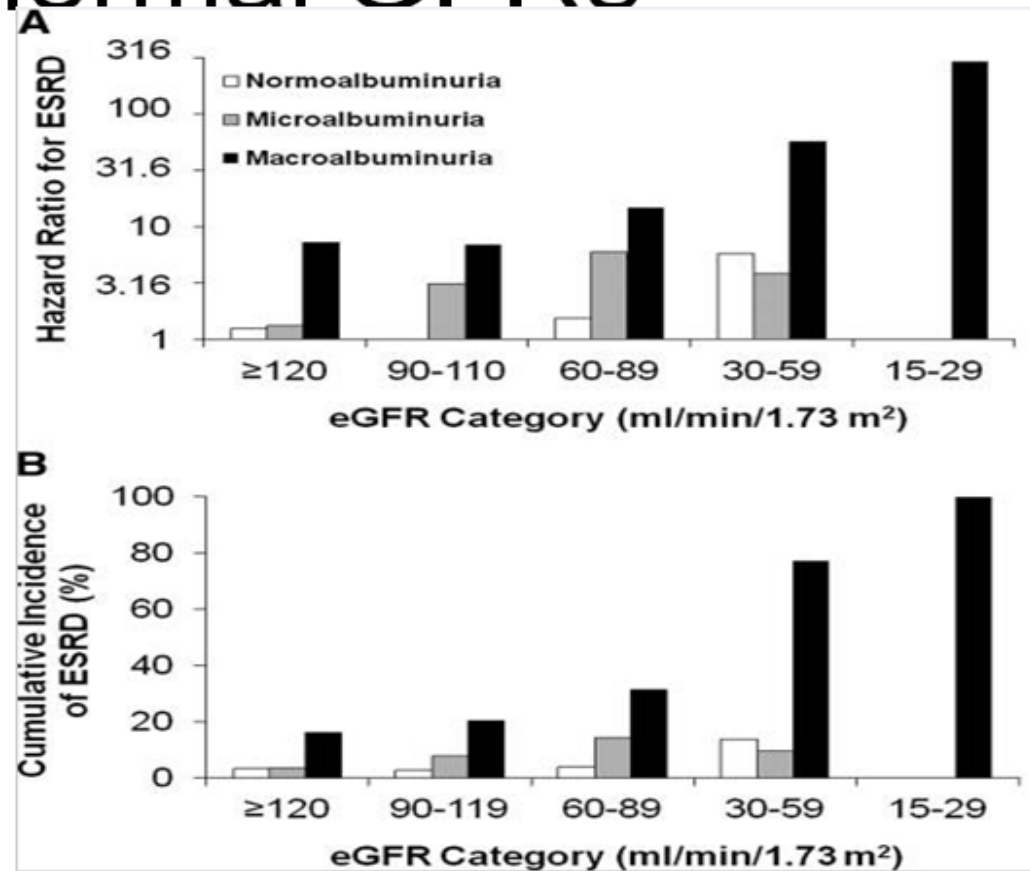
Category	AER (mg/24 h)	ACR (approximate equivalent)		Terms
		(mg/mmol)	(mg/g)	
A1	<30	<3	<30	Normal to mildly increased
A2	30–300	3–30	30–300	Moderately increased ^a
A3	>300	>30	>300	Severely increased ^b

ACR, albumin-creatinine ratio; AER, albumin excretion rate; CKD, chronic kidney disease.

^aRelative to young-adult level.

^bIncluding nephrotic syndrome (AER usually >2200 mg/24 h [ACR >2200 mg/g; >220 mg/mmol]).

Albuminuria is highly prognostic with normal GFRs



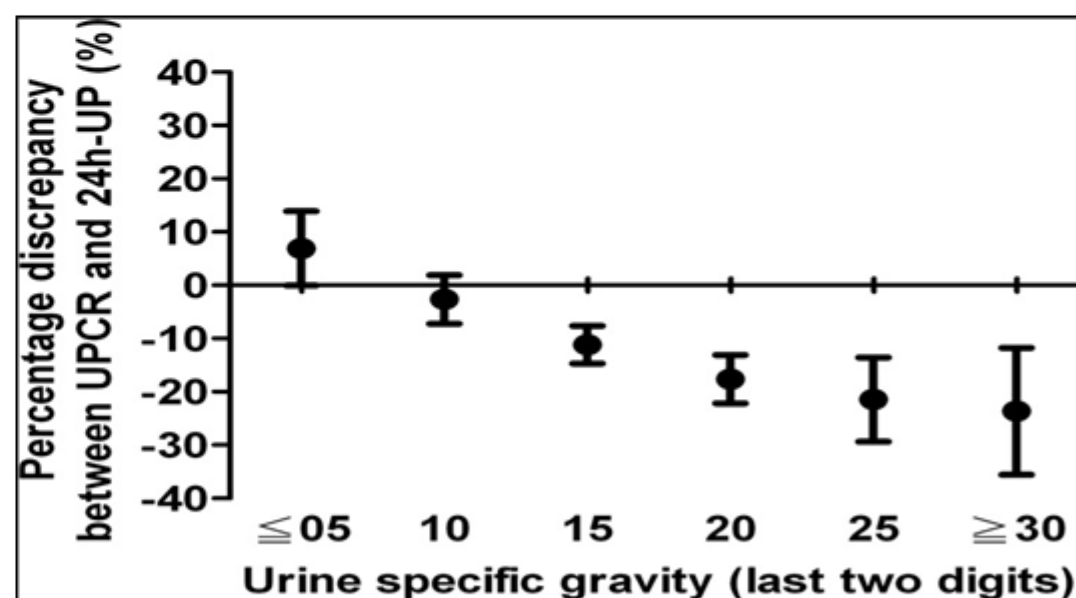
- 2420 diabetic Pima Indians followed between 1982 and 2005
- baseline urine ACR very strongly predictive of future risk of ESRD

Berhane et al. CJASN 2011

Pitfalls in use of random urine ACR levels

- day to day variability of up to 30%
- circadian pattern, lower in am, higher in pm
- transient factors can increase ACR
 - Fever/infection
 - Vigorous exercise
 - Acute severe elevation in BP or BG
- analytic issues with very dilute or concentrated urine

Concentrated and dilute urines



Is this diabetic nephropathy?

Stages of Diabetic Nephropathy by Level of Urinary Albumin Level			
Stage of nephropathy	Urine dipstick for protein	Urine ACR (mg/mmol)	24-hour urine collection for albumin
Normal	Negative	<2	<30 mg/day
Microalbuminuria	Negative	2-20	30-300 mg/day
Overt nephropathy	Positive	>20 >67	>300 mg/day >1,000 mg/day

Values are for urinary albumin, not total urinary protein, which will be higher than urinary albumin levels. ACR results may be elevated with conditions other than diabetic nephropathy (see text and Table 4).

ACR, albumin to creatinine

Factors Favouring Classical Diabetic Nephropathy vs. Alternate Diagnoses	
Favours Diabetic Nephropathy	Favours Alternate Renal Diagnosis
Persistent albuminuria	Extreme proteinuria (>6 g/d)
Bland urine sediment	Persistent hematuria (micro- or macroscopic) or active urinary sediment
Slow progression of disease	Rapidly falling eGFR
Low eGFR associated with overt proteinuria	Low eGFR with little or no proteinuria
Other complications of diabetes present	Other complications of diabetes not present or relatively not as severe
Known duration of DM >5 years	Known duration of diabetes <5 years
	Family history or nondiabetic renal disease (e.g. polycystic kidney disease)
	Signs or symptoms of systemic disease

eGFR, estimated glomerular filtration rate.

Source: Diabetes Canada 2026

Back to Case

- So we need to repeat urine ACR at least once
 - Repeat random urine ACR is 35 mg/mmol
 - Recall urine dip negative for blood
 - No clinical features suggestive of other disease
 - Consider SPEP for older patients
 - ACR <60 mg/mmol and GFR preserved so doesn't need nephrology referral at this time

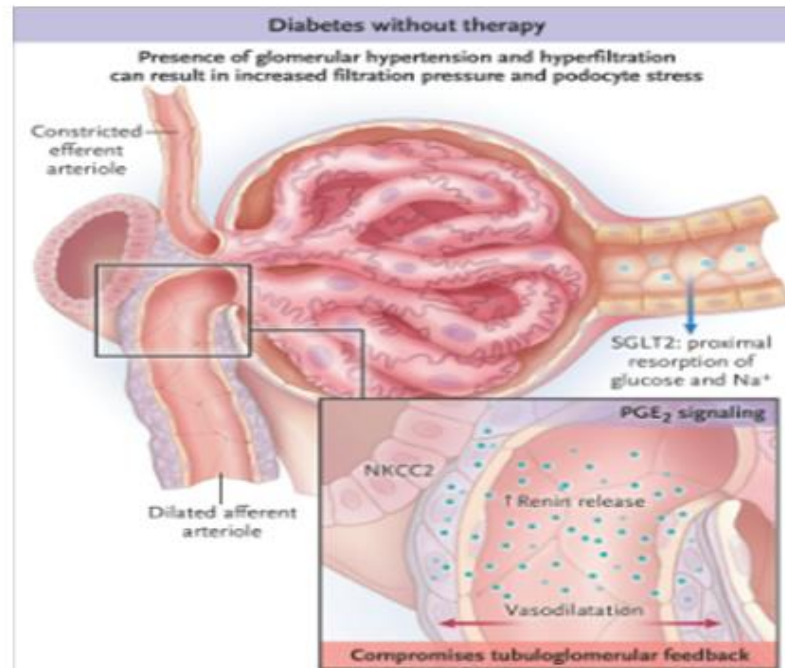
Question 2

- What should I do about his BP management
 1. Add ACE-I
 2. Add ARB
 3. Stop indapamide and add ACE-I
 4. Stop indapamide and add ARB
 5. None of the above

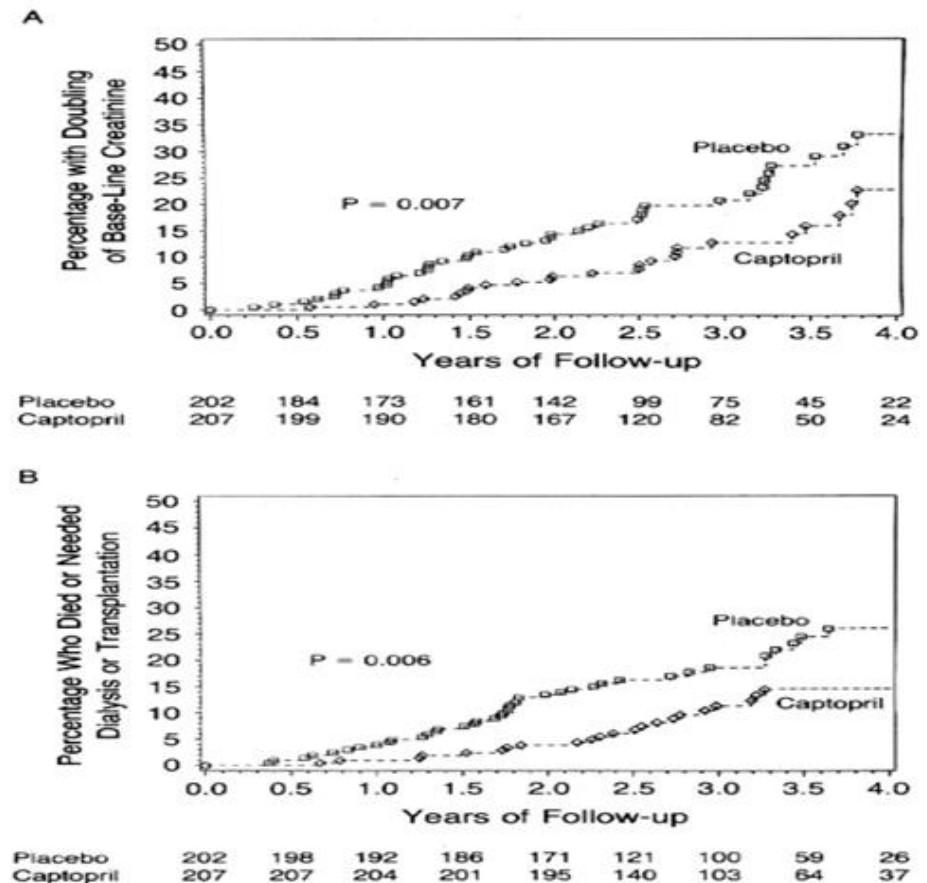
BP Target in Diabetes

- Diabetes Canada:
 - <130/80
- Hypertension Canada:
 - <130/80
- SPRINT study did not include diabetics

Captopril in type 1 diabetes and nephropathy

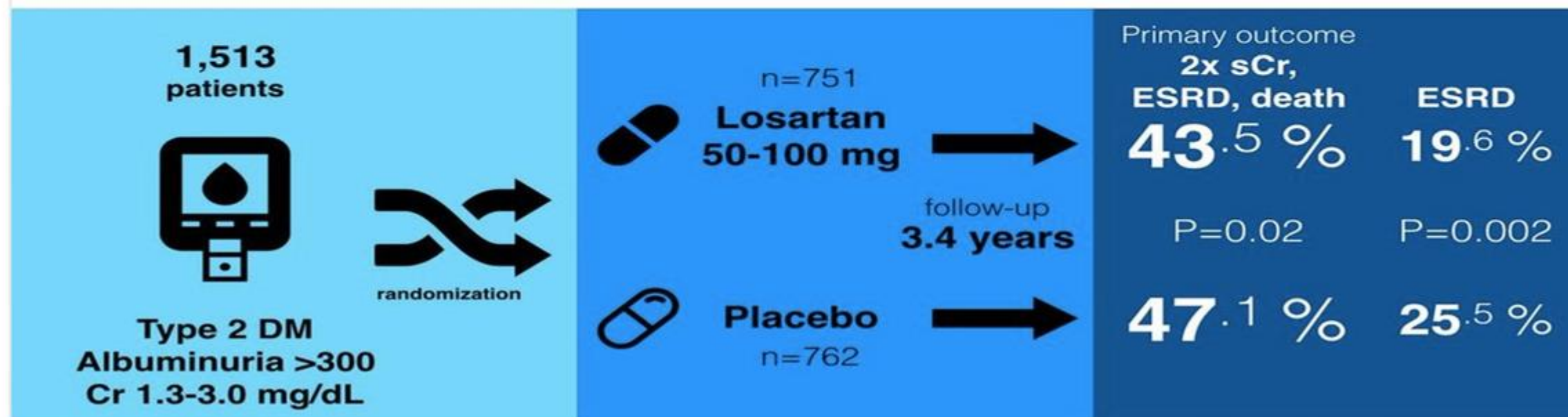


Lewis et al. NEJM 1993



ARB studies in type 2 DM and nephropathy

Effects of Losartan on Renal and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Nephropathy (RENAAL)



Other observations from RENAAL

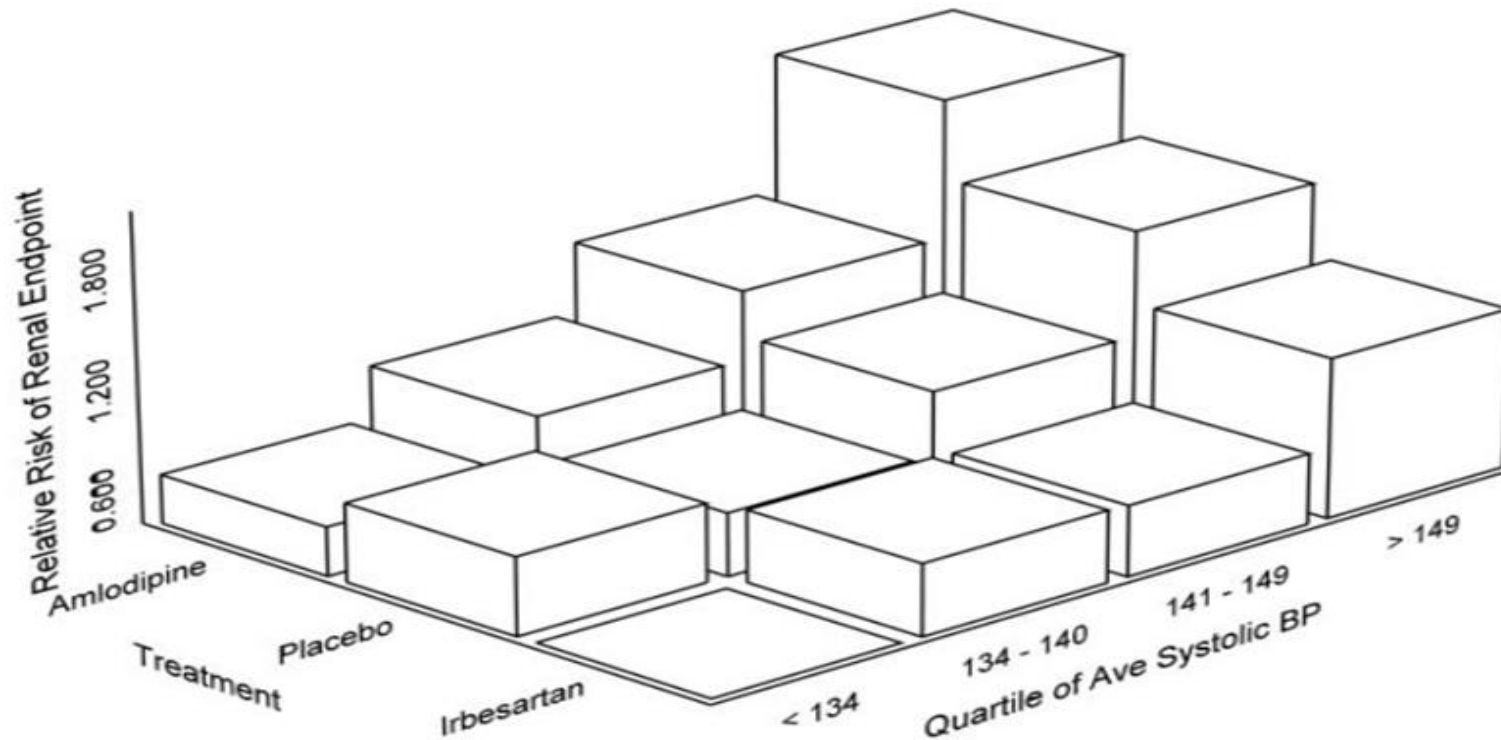
Table 4. ESRD risks by albuminuria and SBP reduction at month 6 from baseline^a

Variables	N	Event (Rate)	Adjusted HR (95% CI)	P
Reduction in ALB				
< -30%	384	95 (85.9)	3.50 (2.49 to 4.94)	<0.000
-30 to 0%	234	62 (96.5)	2.11 (1.49 to 3.01)	<0.000
0 to 30%	326	88 (96.7)	1.64 (1.20 to 2.24)	0.002
≥30%	484	78 (53.8)	1.00	

Changes in GFR slope in RENAAL

- -4.4 vs -5.2 mL/min/1.73m²/yr in losartan vs placebo group
- Delta of 0.8 mL/min/yr vs placebo

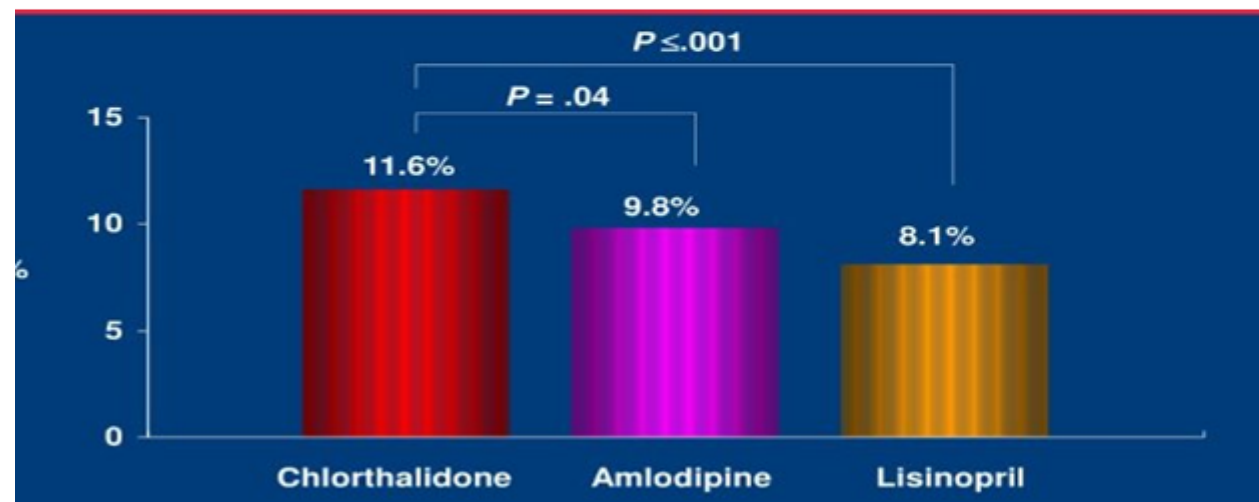
BP control as important as choice of agent



Post hoc analysis of IDNT by Pohl et al. JASN 2005

Thiazides and ACE-I and new onset diabetes

ALLHAT



HOPE

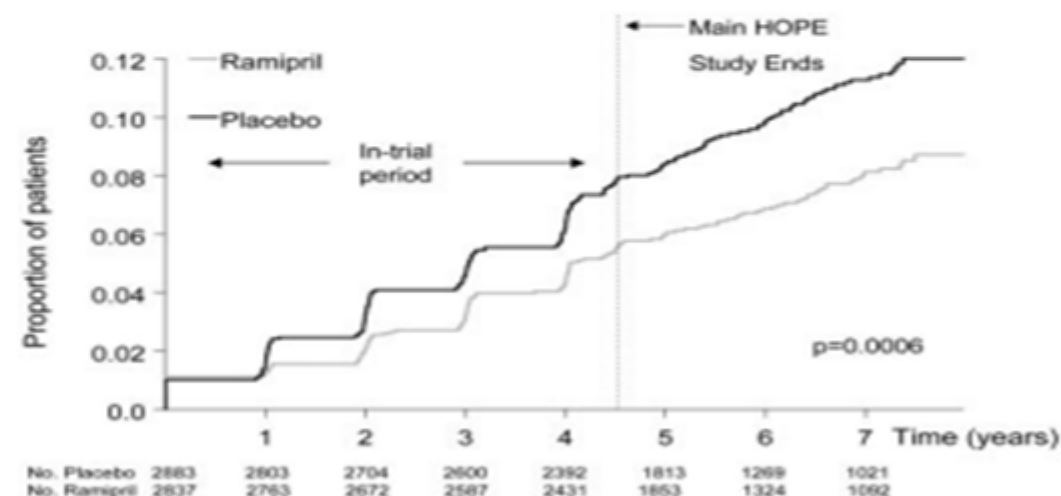
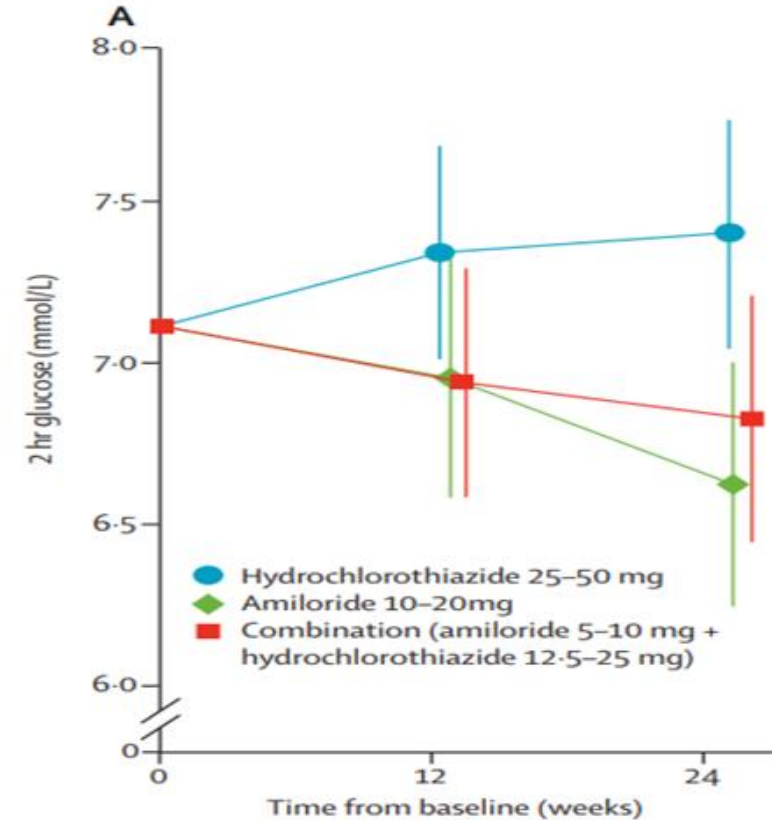
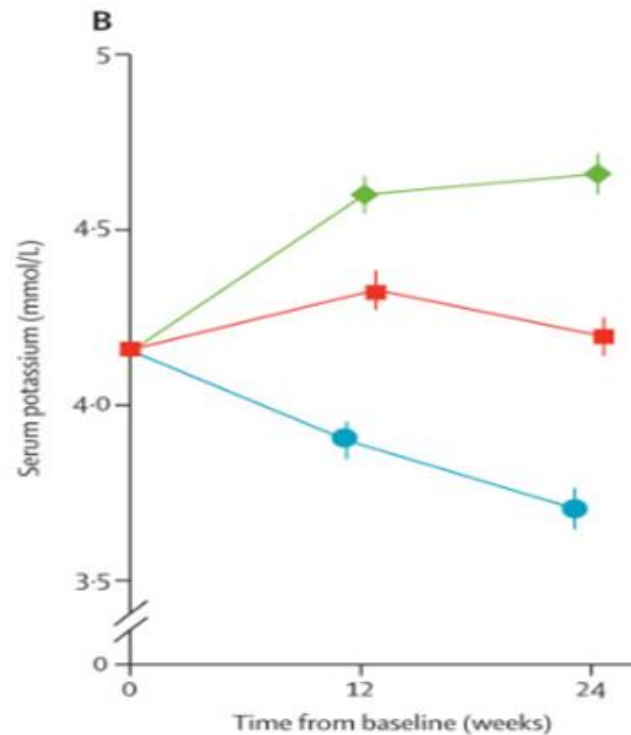


Figure 4. Kaplan-Meier estimates for the outcome of the development of diabetes in the ramipril and placebo groups in the centers continuing in the study extension.

Pathway 3 study

- Randomized 441 patients to 3 diuretic regimes
- 75 g OGTT at 12 and 24 weeks



Brown et al. Lancet Diab 2016

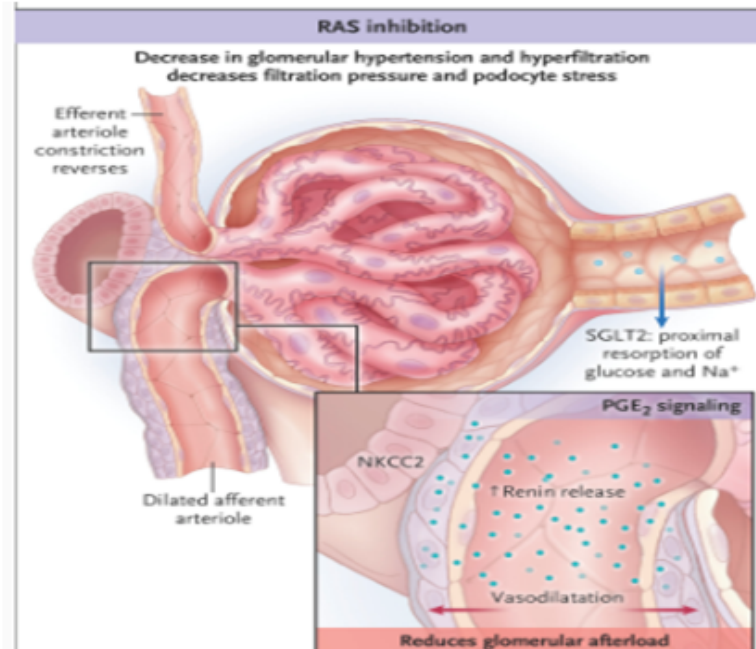
Case

- Stopped indapamide and added candesartan 16 mg, added metformin 500 mg bid
 - 4 weeks later:
 - BP 125/80
 - ACR 28 mg/mmol, Cr 77 umol/L, K 4.8 mmol/L
 - HbA1C 6.8%

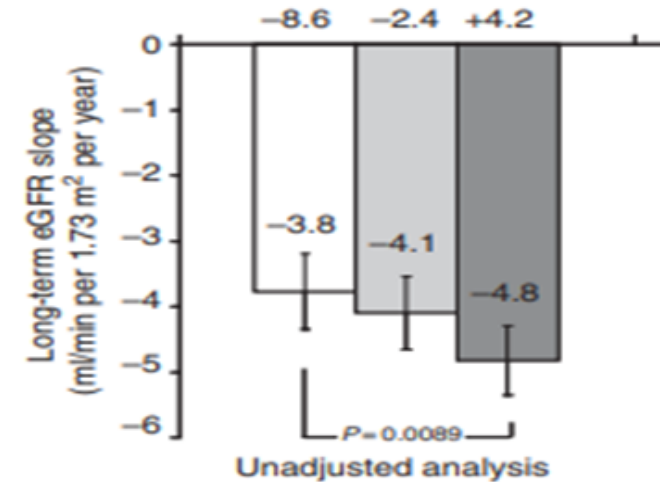
Question 3

- Serum creatinine has risen by almost 25%, what should I do first:
 1. Stop candesartan, put him back on indapamide
 2. Reduce dose of candesartan,
 3. Get a CT angio to rule out renal artery stenosis
 4. Nothing, this is great!

We expect Cr to rise in diabetic nephropathy with RAS blockade



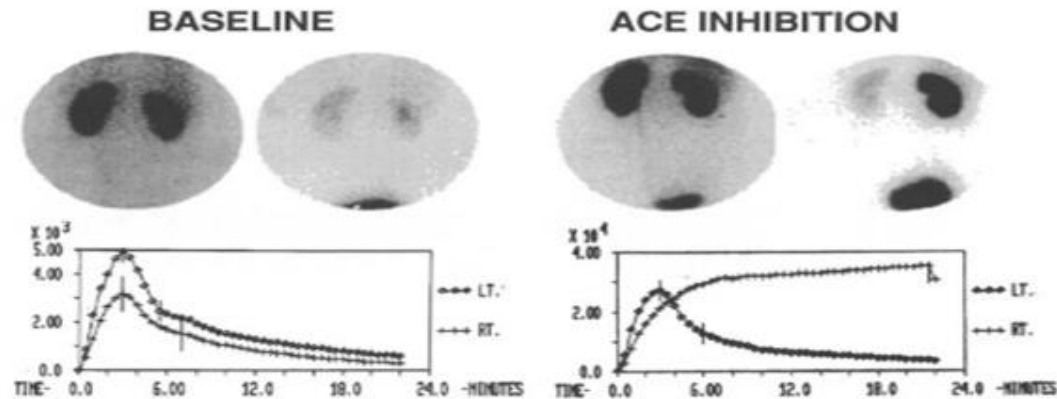
- Post hoc analysis of RENAAL showed greater initial fall in GFR predicted better long term preservation of renal function



Holtkamp et al. Kidney Int 2011

What about Renal Artery Stenosis

Captopril renal scan – historical interest



What about bilateral RAS?

- Relatively rare, usually impaired renal function at baseline
- Often hypervolemic
- Median rise in Cr 38% post ARB (Clin Nephrol 1998)

Guidelines for checking K and Cr post ACE-I or ARB

- Most sources state 4 weeks
 - Not evidence based
 - Will usually see rise in Cr and/or K by 4 weeks but question is the relevance
- Rise of >25% in Cr
 - Don't worry if GFR still normal
 - If GFR low then repeat, if any worse then review benefits of RAS blockade for this patient

Guidelines for checking K and Cr post ACE-I or ARB

- Potassium rise:
 - Risk factors
 - Baseline Cr
 - MRA use
 - Age
- 5.5 mmol/L or greater, reduce dose and/or
 - Add diuretic
 - K binder
- 6 mmol/L stop

Summary

- Diabetic kidney disease is characterized by hyperfiltration, progressively increasing albuminuria followed by a progressive decline in GFR
- ACE-I and ARB reduce the risk of ESRD among those with diabetic nephropathy
- Reduction in albuminuria predicts reduced risk of ESRD
- Even with RAS blockade diabetic nephropathy still has a high risk of progression to ESRD