Chronic kidney disease & diabetes

Dr Sagen Zac-Varghese - Lister Hospital Stevenage

Dr Apexa Kuverji - University Hospitals of Leicester

Learning Outcomes

- 1) To understand how to manage diabetes in people with CKD
- 2) To understand the limitations of HbA1c as a proxy of glucose control in people with diabetes and HbA1c
- 3) To be confident in adjusting insulin in people with diabetes and CKD
- 4) To understand the risks and benefits of novel treatments in diabetes and CKD
- 5) To be aware of the landmark trials of SGLT2i and GLP1-RA therapies in people with diabetes and CKD

Additional learning outcomes for you

Layout of workshop

- Split into 3-4 groups – each group has a case study
- Spend 5 minutes discussing the case studies to present
- Present the case to the group and discussion, linking back to learning outcomes

Case 1

- 69 year old male
- PMH: T2DM on Insulin for >20 years
- CABG (IHD), Essential HTN, AF, LV dysfunction

- K 4.4, Urea 8.6, Creatinine 193, eGFR 30mls/min
- Urine PCR 632mg/mmol, Urine ACR 357mg/mmol

Drug History

- Amlodipine 5mg OD
- Bumetanide 1mg OD
- Carvedilol 25mg BD
- Humulin M3 17+20 BD
- Rivaroxaban 20mg OD
- Simvastatin 40mg OD

Case 1 - Discussion points

- What is the diagnosis?
- When would you consider referring to renal?
- What are the key medications you would consider prescribing here?

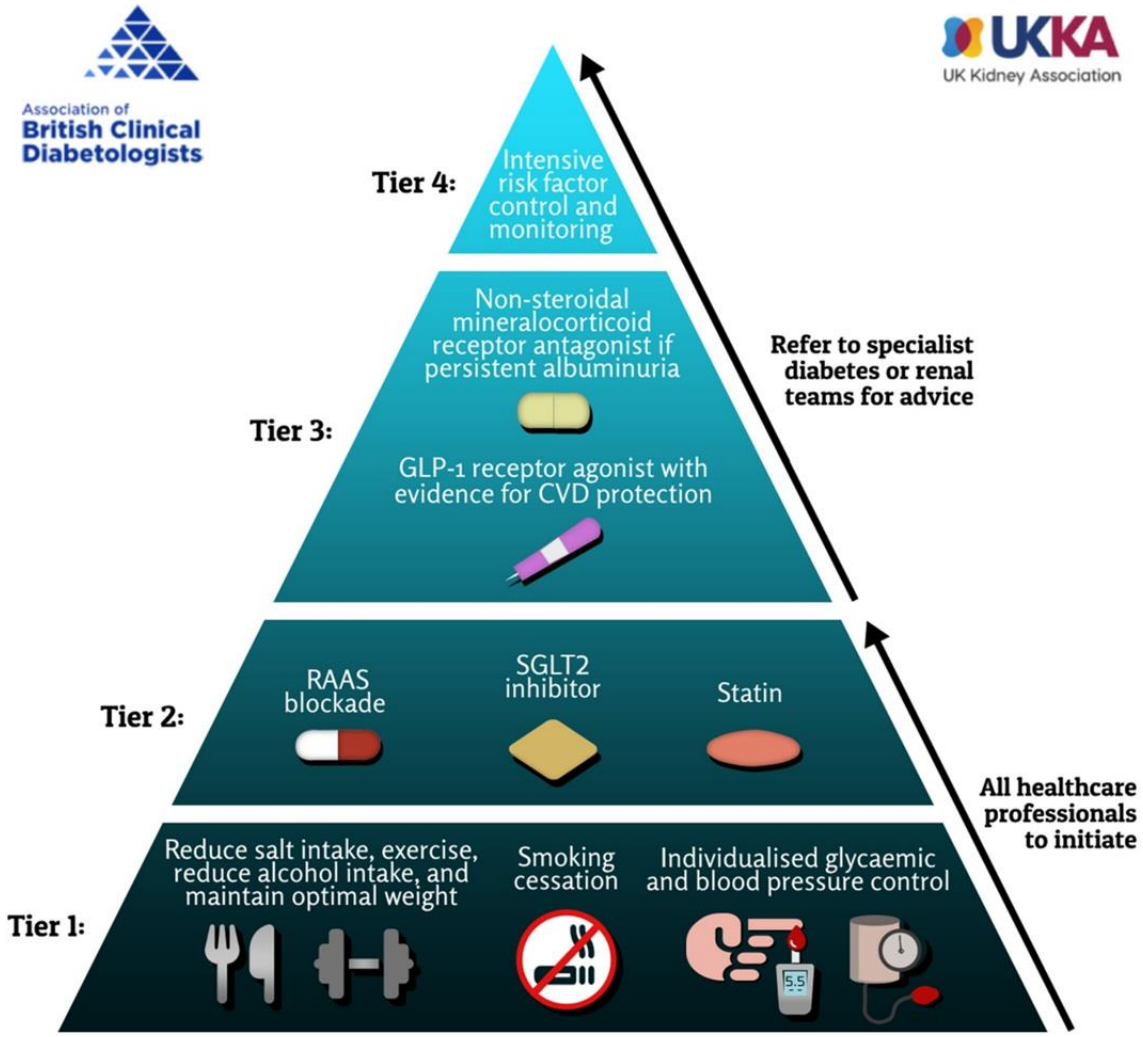
When to refer to Nephrology

- Historically when eGFR <30mls/min
- KFRE 5-year risk of ESKD >5%
  - Use within sensible context
- Accelerated CKD
- Urine ACR > 70mg/mmol
  - unless caused by DM
- Urine ACR >30mg/mmol + haematuria
  - once UTI excluded
- Uncontrolled Hypertension (Hypertension clinic)
- Rare/Genetic disorder of kidneys
- Suspected RAS
- Suspected complication of CKD (anaemia)

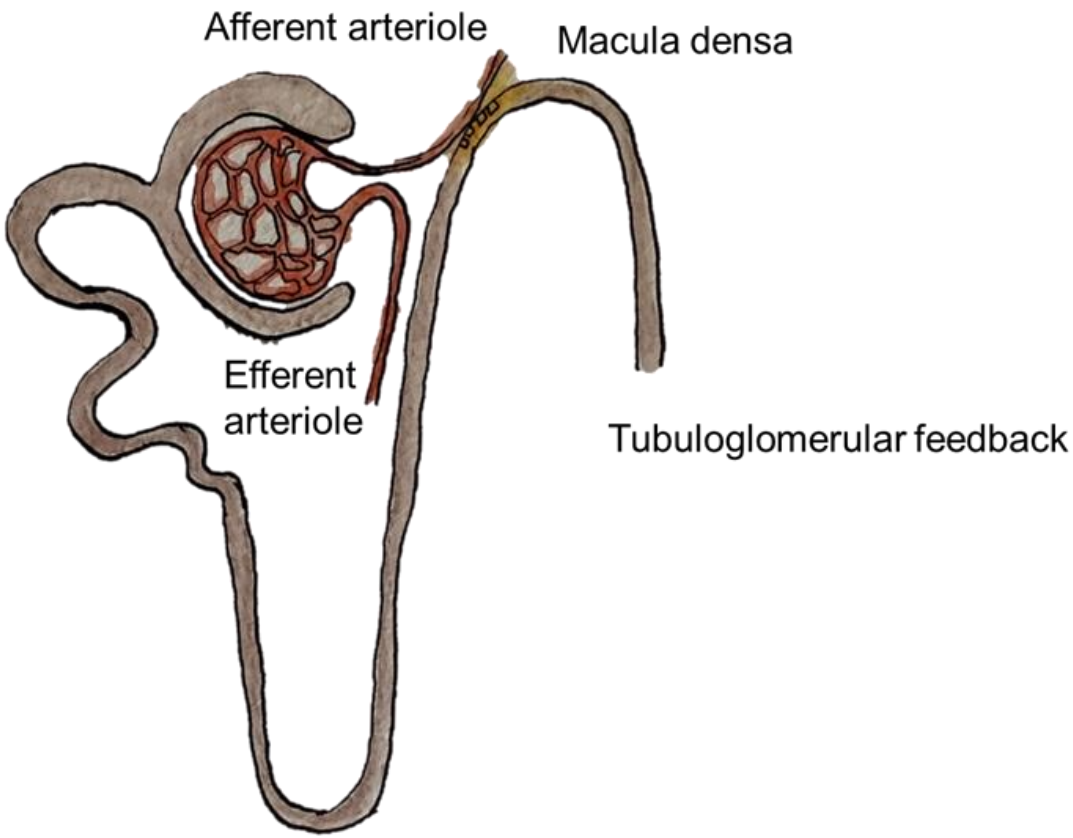
When could it not be DKD?

- Associated haematuria
  - Is it hypertension?
  - Glomerulonephritis
- Well controlled DM with no other microvascular complications (neuropathy/retinopathy)
- Nephrotic Syndrome
  - Although really bad DKD can ultimately get this way
- Myeloma/Amyloid

Key medications for DKD



ACEi/ARB


Afferent arteriole
Macula densa
Efferent arteriole
Tubuloglomerular feedback

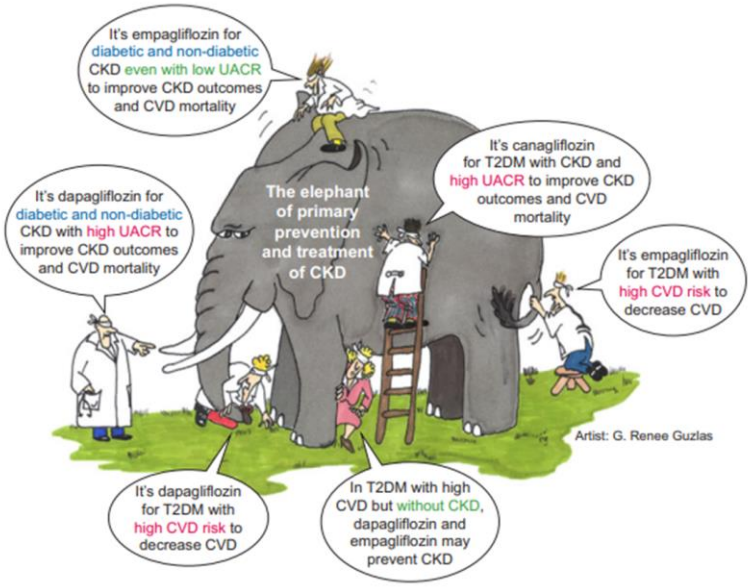
SGLT2i

	CREDENCE	DAPA-CKD	EMPA-KIDNEY
	Canagliflozin	Dapagliflozin	Empagliflozin
Studied	DKD	CKD ± DM	CKD ± DM
eGFR	≥30 to <90	≥25 to <75	≥20 to <90*
Urine ACR	> 30 mg/mmol	≥ 20 mg/mmol	≥200 mg/mmol*
Primary outcome	• Doubling of Cr • Renal death • CVD Death	• 50% decline in eGFR • ESKD • Renal death • CVD death	• 40% decline in eGFR • ESKD • Renal death CVD death

The effect of SGLT2i on kidneys and heart is likely to be a class effect.

When eGFR is < 30, SGLT2i do not affect glucose excretion so will not influence HbA1c.

If the eGFR is > 30 and on insulin reduce this by 20 %, if on gliclazide, reduce this by 50 %.



Dapagliflozin	Empagliflozin	Canagliflozin
Avoid initiating if eGFR < 15	Avoid initiating if eGFR < 20	Avoid initiating if eGFR < 30

Finerenone

Is the eGFR < 60

No

Finerenone 20 mg

Yes*

Finerenone 10 mg

*Do not initiate if eGFR < 25
Stop if eGFR drops < 15 during treatment

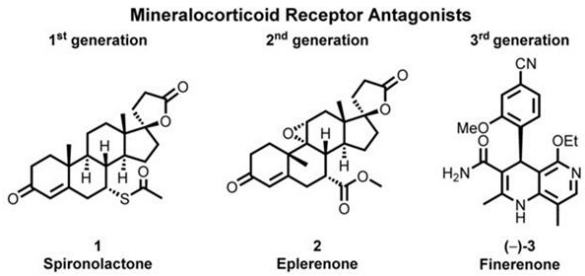
Monitor K^+
4 weeks, then 4 monthly

≤ 4.8 mmol/L

Increase dose maximum 20 mg

≥ 5.5 mmol/L

Reduce dose10 mg
Stop



Case 2

- 41 year old female
- Background:
  - Acute lymphocytic leukaemia – had Bone Marrow transplant in 2012 from her brother
  - Cyclosporin-related nephrotoxicity causing ESKD
  - Kidney transplant from same brother in 2022 (with 99.5% chimerism)
  - T2DM pre-transplant
- BMI 28

Drug history

- Atorvastatin 20 mg OD
- Bisoprolol 2.5 mg OD
- Dapagliflozin 10 mg OD
- Gliclazide 160+ 120 mg BD
- Levothyroxine 100 mcg OD
- Linagliptin 5 mg OD
- Penicillin V 500 mg BD
- Phosphate (Joulies) Liquid 15 ml OD
- Tresiba 100 units/ml Flexpen 46 units OD

- HbA1c 11.3%
- On Tresiba 46 units OD and uptitrating according to CBGs every 3 days.
- Advised to start Trulicity/Ozempic but currently not available

Case 2 – Discussion points

- What factors need to be taken into consideration when uptitrating diabetic treatment in transplant patients?
- How would you treat poor diabetic control in this patient?

Immunosuppression

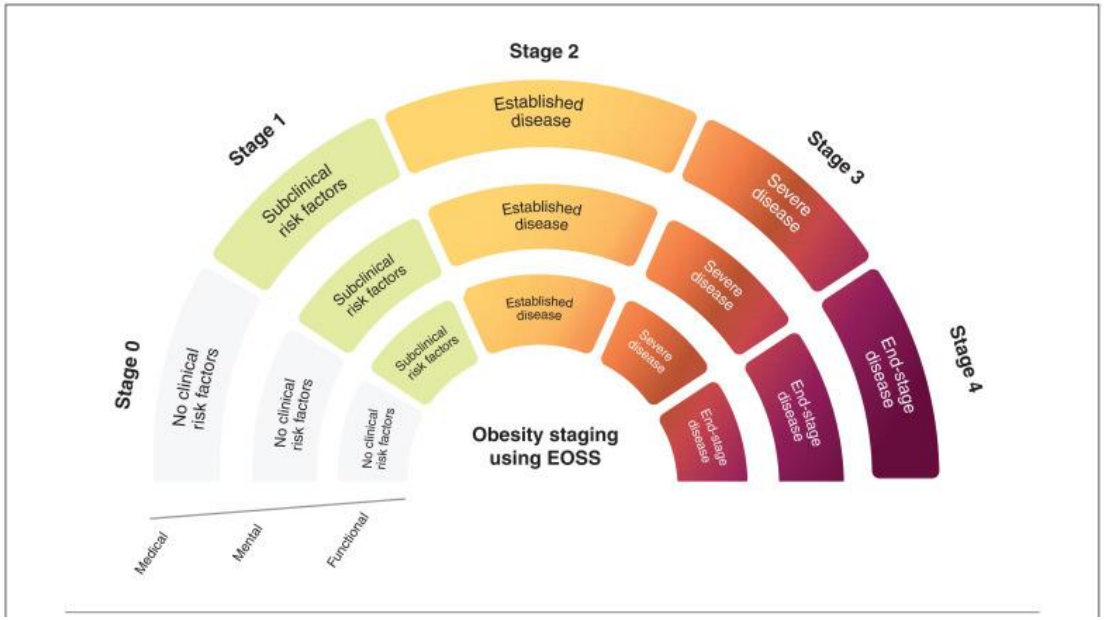
- Transplant Immunosuppression
  - Steroids
    - Increase insulin resistance
    - Increase hepatic gluconeogensis
  - CNI – careful monitoring
    - Impair insulin secretion
    - Cause pancreatic B-cell apoptosis
    - Increase hepatic insulin resistance
  - Anti-metabolite – SE's include hyperglycaemia (mechanism unclear)
- Chimerism in this case

A note on Post-Transplant DM

- Immunosuppression plays a key role
  - Steroids reduced to 5mg OD by 6 weeks (as long as no rejection)
  - CNI dose targets reduce at 6 months
- As kidney function fluctuates drastically, medications needs to be adjusted frequently.
- Once stable – can consider SGLT2i/ Metformin/GLP-1 Agonists etc.

Drugs & weight management

1. Agree weight loss expectation
2. Diet and nutrition
3. Exercise
4. Medications
5. Bariatric surgery



Case 3

- 30 year old male
- PMH: T1DM with retinopathy & macula oedema
- BMI 34
- Drug History
  - Amlodipine 10 mg OD
  - Atorvastatin 20 mg OD
  - Doxazosin 4 mg BD
  - Lyumjev cartridge 0.5units TDS
  - Ramipril 2.5mg OD
  - Sodium Bicarbonate 1g BD
  - Tresiba cartridge 38 units OD
  - Roxadustat 20mg Three per week

Blood & urine test results

Date	K	Urea	Creatinine	eGFR	uPCR	uACR
Feb 2024	5.0	22	300	23	746.5	423
April 2024	6.0	21.7	320	21	643.3	359
May 2024	4.6	21.9	332	20		
July 2024	4.5	21	335	20		
Aug 2024	5.1	22.2	346	19	615.1	332
Nov 2024	5.1	31.7	403	16	241.3	150
Jan 2025	5.0	24.5	388	17		

Case 3 - Discussion points

- How would you manage hyperkalaemia?
- When do you start preparation for dialysis?
- When would you refer for SPK transplant?

Hyperkalaemia monitoring

Severity of Hyperkalaemia	Clinically well (no AKI)	Unexpected result	Clinically unwell or AKI
MILD K^+ 5.5 – 5.9 mmol/l	Repeat within 14 days	Repeat within 3 days	*Consider if hospital referral is indicated
	Assess for cause (drugs, diet) and address in the community		
MODERATE K^+ 6.0 – 6.4 mmol/l	Repeat within 1 working day**	Repeat within 24 hours	Refer to hospital
	Assess for cause (drugs, diet) and address in the community or hospital		
SEVERE $K^+ \geq 6.5$ mmol/l	**Refer to hospital for immediate assessment and treatment**		
	Assess for cause and address during hospital admission		

Table 5: Interval for repeat blood monitoring following an episode of hyperkalaemia.

UKKA Clinical Practice Guideline-Management of Hyperkalaemia in Adults-Oct 2023

Hyperkalaemia

- Sodium Zirconium Cyclosilicate (Lokelma) or Patiromer is an option in adults for the management of **persistent hyperkalaemia with a confirmed serum K+ ≥ 6.0 mmol/l** in patients with **CKD Stage 3b-5 (not on dialysis) or heart failure** receiving a sub-optimal dose of RAASi therapy. (1A)
- Secondary care only

Preparation for kidney replacement therapy

eGFR (mls/min)	General measures	Transplantation	Dialysis
20-30	KFRE discussions		
<20	Weight loss if BMI>37 Consider SPK transplantation (BMI<32)	Request investigations Discuss LDTx	Discussions about dialysis
15	Manage complications of CKD Consider parathyroidectomy if required	Refer to transplant work up clinic	Information of modalities (MDT)
12-10	Avoid illnesses Continue	Active on transplant register	Refer for access
<10			Start dialysis therapy

SPK transplantation

- Insulin treated DM
- Should have T1DM or DM secondary to pancreatectomy / pancreatitis.
- Confirmed C-peptide negativity in presence of glucose more than 10 mmol/l.
- Pancreas transplantation with T2DM must have calculated BMI of </= 30 kg/m2 at time of listing
- If Pancreas/Islet transplant alone must have at least two severe hypoglycaemic episodes, within the last 2 years (and have disabling hypoglycaemia according to a diabetologist)
- For simultaneous kidney pancreas/islet transplant, must be receiving dialysis or eGFR of 20mls/min or less at the time of listing.
- For islet after kidney transplant- should have a history of severe hypoglycaemia within last two years or HbA1C > 53 mmol/mol at time of listing.

Case 4

- 64 year old male with T2DM on maintenance haemodialysis
- PMHx
  - Peripheral vascular disease
  - Treated spinal TB
  - Essential HTN
  - Failed transplant
  - Previous parathyroidectomy
- Last HbA1c 68mmol/mol (8.4%)
- Pre-dialysis CBG 5.7-8.9
- Post-dialysis CBG 5.9-9.5

Drug history

- Adoport 4 mg BD
- Alfacalcidol 1 mcg OD
- Aspirin 75 mg OD
- Atorvastatin 40 mg OD
- Calvive 2000 mg / 2000mg / 3000mg TDS
- Citalopram 20 mg OD
- Humulin I Kwikpen 26+12 units BD
- Lansoprazole 15 mg OD
- Linagliptin 5 mg OD
- Lokelma 5 g x4/wk
- Prednisolone 5mg OD
- Sevelamer 800 mg TDS
- Darbepoetin - Aranesp 40 mcg Weekly IV

Case 4 - Discussion points

- What is the best way to determine glucose control in people on maintenance haemodialysis?
- What factors need to be considered when uptitrating treatment in people on haemodialysis?

Continuous blood glucose monitoring

CGM versus HbA1c versus fructosamine/glycated albumin

1. Look at summary – i.e. check for sufficient data
2. Review the report with the patient – correlate with meals/ treatment/activity
3. Evaluate TIR, hypos, glycaemic variability
4. Interrogate hypos – exercise, overcorrection, vomiting.
5. Look at hyperglycaemia
6. **Agree on plan with patient**

Glucose control on dialysis

- Aim for BG 6 to 12
- U shaped curve glycaemia/mortality for dialysis
- Hypoglycaemia = main risk

- Insulin requirement falls by 50 % when eGFR < 10

- Both insulin and glucagon is cleared by dialysis

- Euglycaemic clamp studies – show that insulin requirement is 25 % less on dialysis days so reduce insulin by 25 % on dialysis days

Signposts

- Kidney care UK potassium
  - https://kidneycareuk.org/get-support/healthy-diet-support/lowering-your-potassium-levels/
- Kidney Risk Failure Equation
  - https://kidneyfailurerisk.co.uk/
- JBDS guidelines
- UKKA guidelines
  - UKKA Clinical Practice Guideline – Management of Hyperkalaemia in Adults – October 2023 (ukkidney.org)
- Transplantation
  - Policies and guidance - ODT Clinical - NHS Blood and Transplant