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Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and their role in CKD patients

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Aims and objectives

Aim:

To increase knowledge of Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and their role in CKD patients.

Objectives:

1. Understand GLP-1s - what they are and how they work
2. The role of GLP-1s in CKD patients
3. Suitability and safety considerations
4. Side effects and dosing in CKD patients

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Glucagon-like peptide-1 receptor agonists GLP-1 RAs- what are they?

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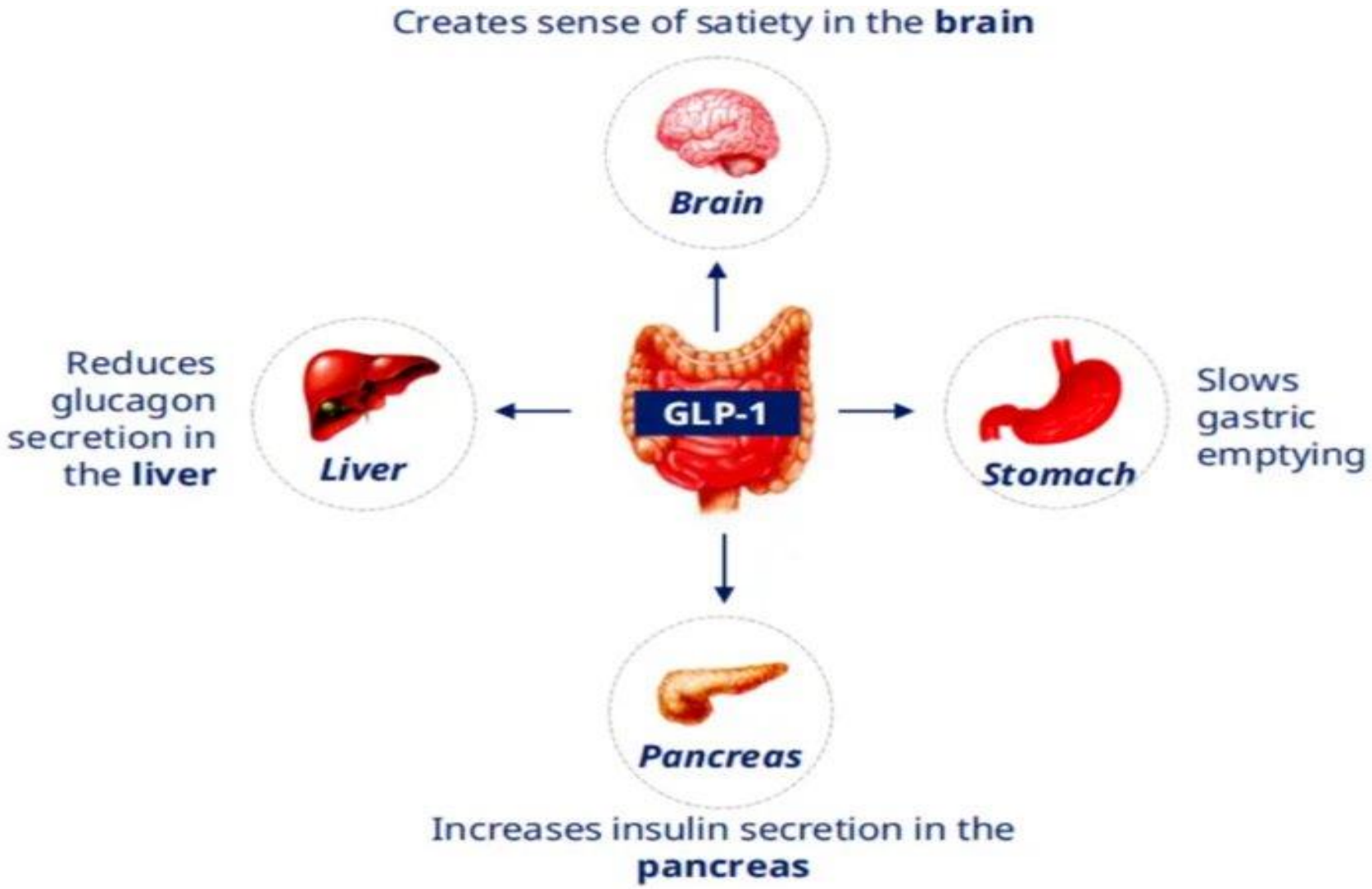
1984	• the first GLP-1 was discovered
2005	• Exenatide was the first GLP-1 commercially available to treat T2DM, followed by liraglutide, semaglutide, dulaglutide and tirzepatide.
2014	• liraglutide was first GLP-1 marketed for weight loss
2021	• semaglutide available for weight loss
2023	• – first GLP-1/GIP tirzepatide available for weight loss
2026	• + beyond… more and more trials showing extra benefits and new versions in development

GLP-1 RAs

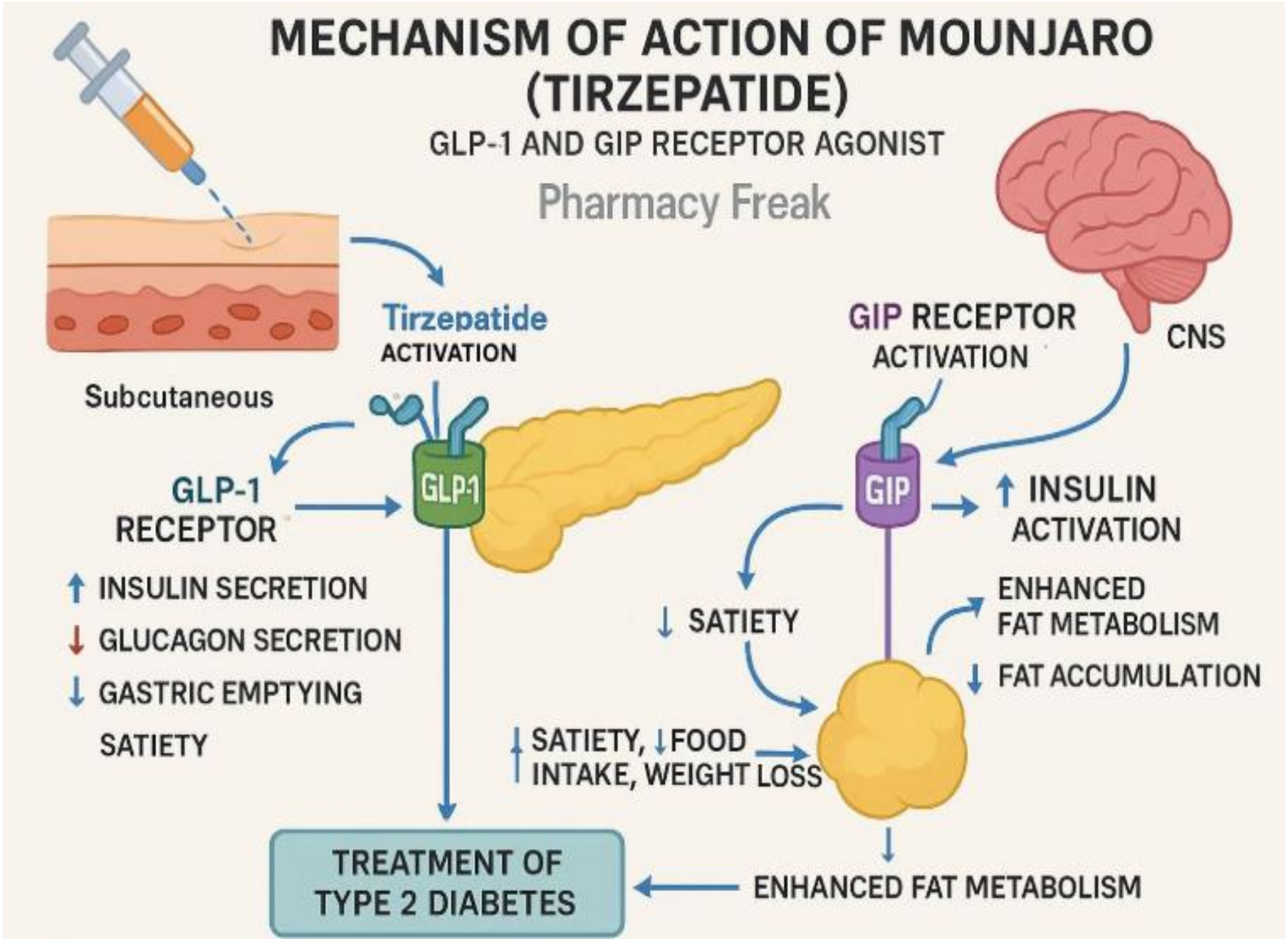
Five GLP-1RAs are available in the UK:

- dulaglutide,
- exenatide,
- liraglutide,
- **semaglutide (Wegovy/Ozempic /Rybelsus),**
- **tirzepatide (Mounjaro/Zepbound)***

GLP-1 mechanism of action:



Novo Nordisk 2023


MECHANISM OF ACTION OF MOUNJARO
(TIRZEPATIDE)
GLP-1 AND GIP RECEPTOR AGONIST
Pharmacy Freak
Subcutaneous
Tirzepatide
ACTIVATION
GIP RECEPTOR
ACTIVATION
CNS
GLP-1
RECEPTOR
GLP-1
GIP
INSULIN
ACTIVATION
INSULIN SECRETION
GLUCAGON SECRETION
GASTRIC EMPTYING
SATIETY
SATIETY
ENHANCED
FAT METABOLISM
FAT ACCUMULATION
SATIETY, FOOD
INTAKE, WEIGHT LOSS
TREATMENT OF
TYPE 2 DIABETES
ENHANCED FAT METABOLISM

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Suitability and safety in CKD patients

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Current obesity guidelines

Semaglutide for managing overweight and obesity(TA875) March ’23

Semaglutide is recommended as an option for weight management, alongside a reduced-calorie diet and increased physical activity in adults, if:

•it is used for a maximum of 2 years, and within a specialist weight management service providing MDT (including but not limited to tiers 3 and 4), and

•they have at least 1 weight-related comorbidity and:

•a BMI of at least 35.0 kg/m^2

Tirzepatide for managing overweight and obesity (TA1026) Dec ‘24

Tirzepatide is recommended as an option for managing overweight and obesity, alongside a reduced-calorie diet and increased physical activity in adults, only if they have:

•an initial body mass index (BMI) of at least 35 kg/m^2 and

•at least 1 weight-related comorbidity

****Updated June ‘25 + more expected June ‘26 + March ‘27**

The problem with current guidelines

NICE obesity guidelines do not include renal patients - as a subgroup or comorbidity.

Not commonly prescribed in patients with ESKD living with obesity…….Why?

….potentially due to lack of understanding in this group

Most GLP1-s are not recommended in ESKD.

No large clinical trials specifically on CKD patients **without diabetes**.

So…are GLP-1s safe in renal patients?

- Not metabolised by the kidney.
- CKD does not appear to affect tolerability or safety.
- No evidence they affect tacrolimus or other commonly used immunosuppressants.
- Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Diabetes Management in CKD prioritised their use in CKD patients with T2DM since 2022.
- They can be prescribed to kidney patients (inc transplant) for weight loss, cardiovascular risk reduction and T2DM with minimal risk.

Breaking news…..

6 October 2025

GLP-1 receptor agonists: prescribing in CKD and supporting patient access

The UK Renal Pharmacy Group has issued guidance recommending timely access to GLP-1 receptor agonists (GLP-1 RAs) for people with chronic kidney disease (CKD), including those with kidney transplants.

Evidence shows that reduced kidney function does not affect the safety or tolerability of GLP-1 RAs. These medicines can be prescribed safely for weight loss, cardiovascular risk reduction and/or type 2 diabetes in patients with CKD, including those on dialysis and post-transplant, as they are not metabolised by the kidney. Standard dosing and titration schedules can generally be followed.

GLP-1 RAs—such as semaglutide and tirzepatide—have demonstrated kidney and cardiovascular protective effects in large clinical trials, leading to their prioritisation in the **KDIGO Clinical Practice Guideline for Diabetes Management in CKD**. The UK Renal Pharmacy Group highlights that kidney patients should be considered a priority group for GLP-1 RA treatment, given the potential to slow CKD progression, reduce morbidity and improve outcomes.

This latest document also provides practical advice on safety, monitoring, and counselling for patients, including side-effect management and key considerations for those accessing GLP-1 RAs via private weight-loss clinics.

UK Renal Pharmacy Group/UKKA stance on GLP-1

The UKRPG recommends that renal patients should be considered a priority group for GLP-1 RAs because:

- Large, randomised control trials demonstrate kidney protection in CKD patients **with diabetes.***
- Obesity accelerates kidney function decline in patients with CKD, irrespective of diabetes status.
- Advanced CKD and ESKD is associated with high rates of morbidity and mortality.

Should all CKD patients living with obesity get a GLP-1?

Not straightforward….wraparound care is best!

Not suitable for all patients – exclusions:

- Proliferative diabetic retinopathy
- Pancreatitis
- Family or personal Hx of thyroid cancer
- Eating disorders

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Dosing, side effects and safety

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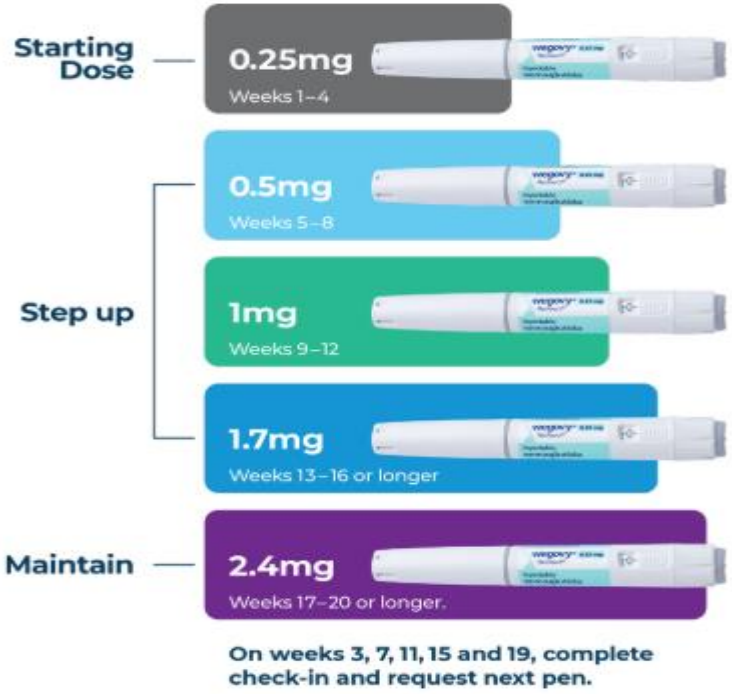
Do we need to reduce the dose?

Pharmacokinetic data shows that:

- Standard starting doses of GLP-1s can be used in kidney patients at all levels of kidney function, including ESKD receiving dialysis and kidney transplant patients.
- Normal titration schedules can usually be followed.

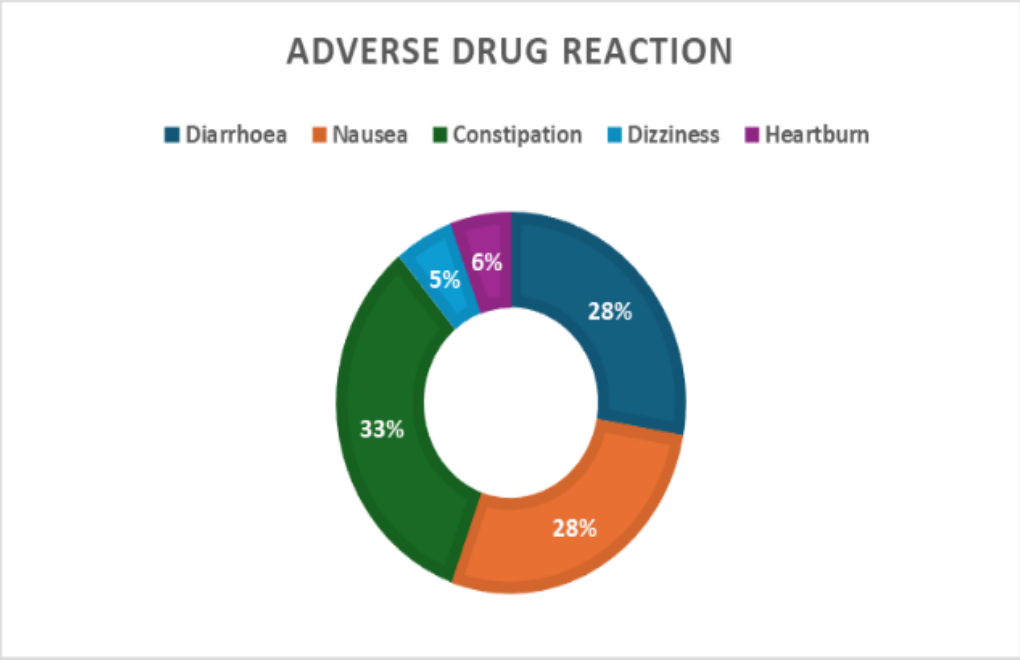


What are the side effects? Do renal patients get more?

Organ class	Very common	Common	Uncommon
Metabolism and nutrition disorders	Hypoglycaemia when used with insulin or sulfonylurea	Hypoglycaemia[a] when used with other oral antidiabetics (OAD) Decreased appetite	
Nervous system disorders		Dizziness Headache	Dysgeusia
Eye disorders		Diabetic retinopathy complications	
Cardiac disorders			Increased heart rate
Gastrointestinal disorders	Nausea Diarrhoea	Vomiting Abdominal pain Abdominal distension Constipation Dyspepsia Gastritis Gastro-oesophageal reflux disease Eructation	

What we learned from KFiT…

- Semaglutide is well tolerated by most renal patients regardless of modality.
- Dosing can be titrated as normal.
- Side effects are comparable to the general population.
- Language matters!
- Wraparound care



Future considerations…

- Examining maintenance doses as part of KFiT. Anecdotal evidence so far but watch this space…
- New oral GLPs in development (oral semaglutide already available)
- Expansion of UK licensing to include renal cohort?? FDA approved semaglutide in patients with T2DM and CKD on the back of FLOW trial*
- MDT led approach- renal patients living with obesity are complex!
- Wraparound care works!

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5. Kidney Disease: Improving Global Outcomes Diabetes Work Group (KDIGO) Clinical practice guideline for diabetes management in chronic kidney disease. Kidney Inter, Suppl. 2020;2020(98):S1–S115. doi: 10.1016/j.kint.2020.06.019.

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Questions?

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