SGLT-2 inhibitors and cardio-renal outcomes

This activity is supported by an unrestricted educational grant from AstraZeneca

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Early intervention of clinicians can lead to slower CKD progression, and thereby delayed dialysis initiation and CV complications — highlighting the link between poor kidney function and high risk of CV complications[1]

CKD prevalence

697.5 million people have CKD; mean global prevalence is **13.4%**[2,3]

CKD is the **12th** leading cause of death[2]

30%-60% of pts with established CVD or presenting with acute CV events have CKD[3]

40% of pts with diabetes have CKD[4]

**Data are underestimates due to lack of screening*

Screening for CKD

The justification of CKD is based on albuminuria and eGFR – both risk factors for CKD and CVD, and used to classify CKD risk levels.

All patients with kidney disease, diabetes, hypertension or other metabolic diseases should be screened for albuminuria[5]

To measure albuminuria, it is preferable to take the **first morning urine sample**

Guideline recommendations on CKD screening

Assessment of CKD using both eGFR and albuminuria should occur at least:

- **once a year**, in pts with certain conditions (e.g. hyperlipidaemia, hypertension, CVD, and diabetes)
- **1-2 times a year**, in pts with mild to moderate CKD
- **3-4 times a year**, in pts with moderate to severe CKD[6]

Guide to Frequency of Monitoring (number of times per year) by GFR Albuminuria Category

GFR categories (ml/min/1.73m²) Description and range				Persistent Albuminuria Categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90	1 if CKD	1	2
	G2	Mildly decreased	60–89	1 if CKD	1	2
	G3a	Mildly to moderately decreased	45–59	1	2	3
	G3b	Moderately to severely decreased	30–44	2	3	3
	G4	Severely decreased	15–29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+

Adapted from Levin and Stevens, 2014

Abbreviations: ACEi, Angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; DKD, diabetic kidney disease; eGFR, estimated glomerular filtration rate; HF, heart failure; pts, patients; SGLT-2i, sodium-glucose cotransporter 2 inhibitor; T2DM, type 2 diabetes mellitus.

References: **1.** Ruggenenti P et al. *JASN* 2012;23:1917-1928. **2.** GBD Chronic Kidney Disease Collaboration. *The Lancet* 2020;395:P709-733. **3.** Hill NR et al. *PLoS ONE* 2016;11: e0158765 **4.** *Gheith* O et al. *J Nephropharmacol* 2016;5:49–56. **5.** Busby DE, Bakris GL. *J Clin Hypertens (Greenwich)* 2004;6:8-12. **6.** Levin A, Stevens PE. *Kidney International Supplements* 2014;85:49-61.

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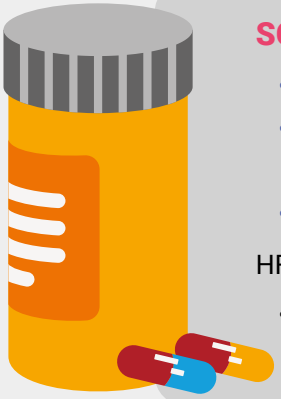
Evidence-based treatments in CKD

ACEis and ARBs shown to protect the kidneys in both (non-)diabetic kidney disease but NOT all pts benefited from these treatments[7]



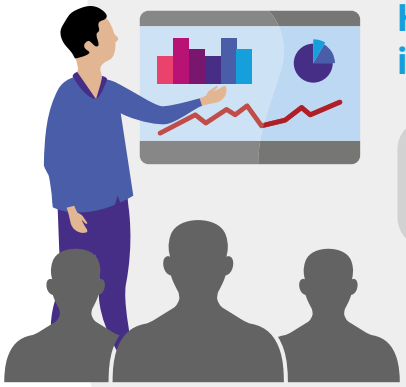
SGLT-2is shown to protect the kidneys in pts with kidney disease[8-10]

- **Dapagliflozin** in DAPA-CKD trial protected the kidney in CKD pts with(out) T2DM
- **Empagliflozin** in EMPEROR trial reduced the risk of kidney failure in pts with preserved kidney function
- **Canagliflozin** in CREDENCE trial protected the kidneys in pts with DKD

HF trials shown protective roles of SGLT-2is against HF in pts with established HF, or CKD

- EMPEROR-reduced, EMPEROR-preserved, and DAPA-HF showed that SGLT-2is slow the progression of kidney function decline in pts with HF

Finerenone a non-steroidal mineralocorticoid receptor antagonist, reduced the risk of kidney failure and HF with DKD, in FIDELIO-DKD and FIGARO-DKD trials[11]



How to encourage patients and clinicians to initiate SGLT-2 inhibitors therapy in patients with CKD

Overwhelming data support the use of SGLT-2is for CKD, however **therapeutic inertia** – *the gap from efficacy to effectiveness* – is a major barrier to their early adoption

To put evidence into clinical practice, **both clinicians and patients** need to

- be informed about the trial outcomes
- initiate these therapies especially when there is an urgency to treat

Ease of implementing SGLT-2 inhibitors

SGLT-2is are

easy to use due to fixed dose combination

well-tolerated with mild adverse events

- Main adverse event is **genital infection** – due to increased glycosuria
- Other adverse events include **volume depletion** and **orthostatic hypotension**[12]

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References: **7.** Zou H et al. *Cardiovasc Diabetol* 2017;16:65. **8.** Davidson JA. *Postgraduate Medicine* 2019;131:251-260. **9.** Heerspink HJL et al. *N Engl J Med* 2020;383:1436–46. **10.** McMurray JVJ et al. *N Engl J Med* 2019; 381:1995-2008. **11.** Shabaka A et al. *Frontiers in Medicine* 2021;8:645187. **12.** Pelletier R et al. *Ther Adv Drug Saf* 2021;12:2042098621989134.