Understanding Diabetic Kidney Disease: Early Detection and Management

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Land Acknowledgement

We are in Mi’kma’ki, the ancestral and unceded territory of the Mi’kmaq. We are all treaty people.

Acknowledge the histories, contributions and legacies of the African Nova Scotian people and communities who have been here for over 400 years.

https://novascotia.ca/abor/aboriginal-people/community-info/

Presenter Disclosure

- Presenter's Name: Jo-Anne Wilson
- I have the following relationships with commercial interests:
  - Funding (Grants/Honoraria): Bayer, Otsuka
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  - I have received no speaker's fee for this learning activity

Commercial Support Disclosure

- This program has received no financial or in-kind support from any commercial or other organization

Abbreviations

ACEi	angiotensin-converting enzyme inhibitor
ARB	angiotensin II receptor blocker
BP	blood pressure
CKD	chronic kidney disease
CV	cardiovascular
DKD	diabetic kidney disease
eGFR	estimated glomerular filtration rate
ESKD	end-stage kidney disease
GLP1RA	GLP-1 receptor agonist
KDIGO	kidney disease improving global outcomes
MACE	major adverse cardiovascular event
nsMRA	non-steroidal mineralocorticoid receptor antagonist
SCr	serum creatinine
SGLT2i	sodium-glucose cotransporter II inhibitor
T2D	type 2 Diabetes
UACR	urine albumin creatinine ratio

Learning Objectives

At the end of this session, participants will be able to:

Understand	care gaps pertaining to DKD screening and detection
Incorporate	guideline recommended pillars of management for DKD
Create	pharmacy care plan based on patient goals and preferences

Road Map

- Why DKD Matters?
- Screening and Detection
- Management Pillars
- Evidence
- Case Vignette
- Resources

Diabetes is the leading cause of CKD

Why DKD Matters?

11 million people in Canada live with diabetes or pre-diabetes

Diabetes contributes to **38%** of kidney failure requiring dialysis

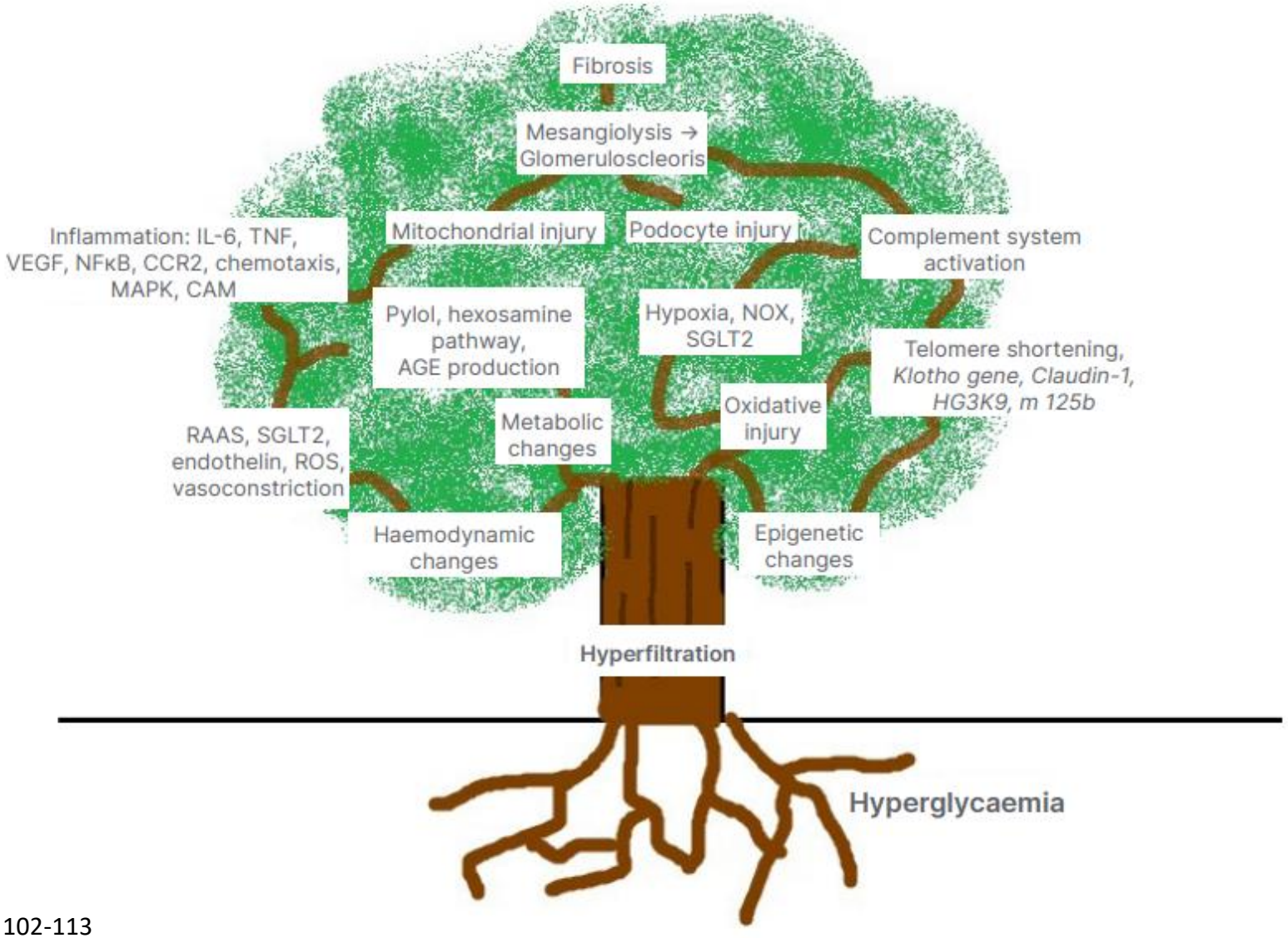
12 X more likely to be hospitalized with ESKD

Kidney disease increases risk of **CVD**

1 in 3 with diabetes have CKD

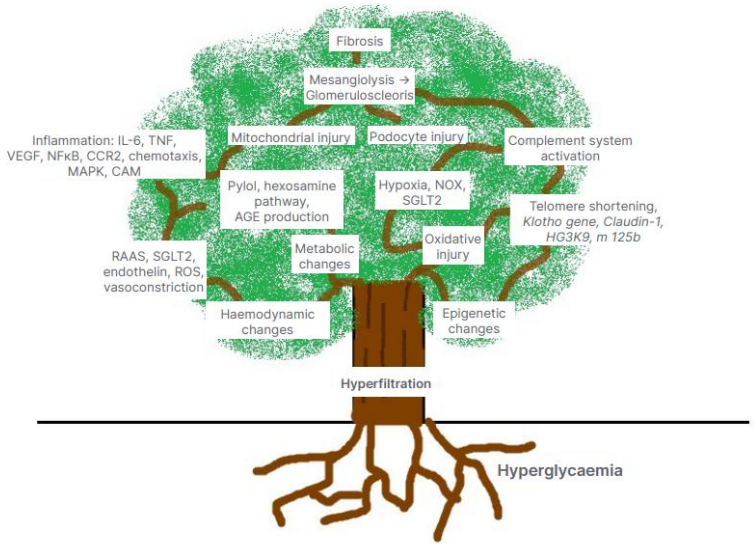
https://kidney.ca/KFOC/media/images/PDFs/Facing-the-Facts-2023-HIghlights-from-the-Annual-Statistics-on-Organ-Donation.pdf;
https://kidney.ca/KFOC/media/images/PDFs/Why-Kidney-Disease-Should-Matter-to-You_2025.pdf

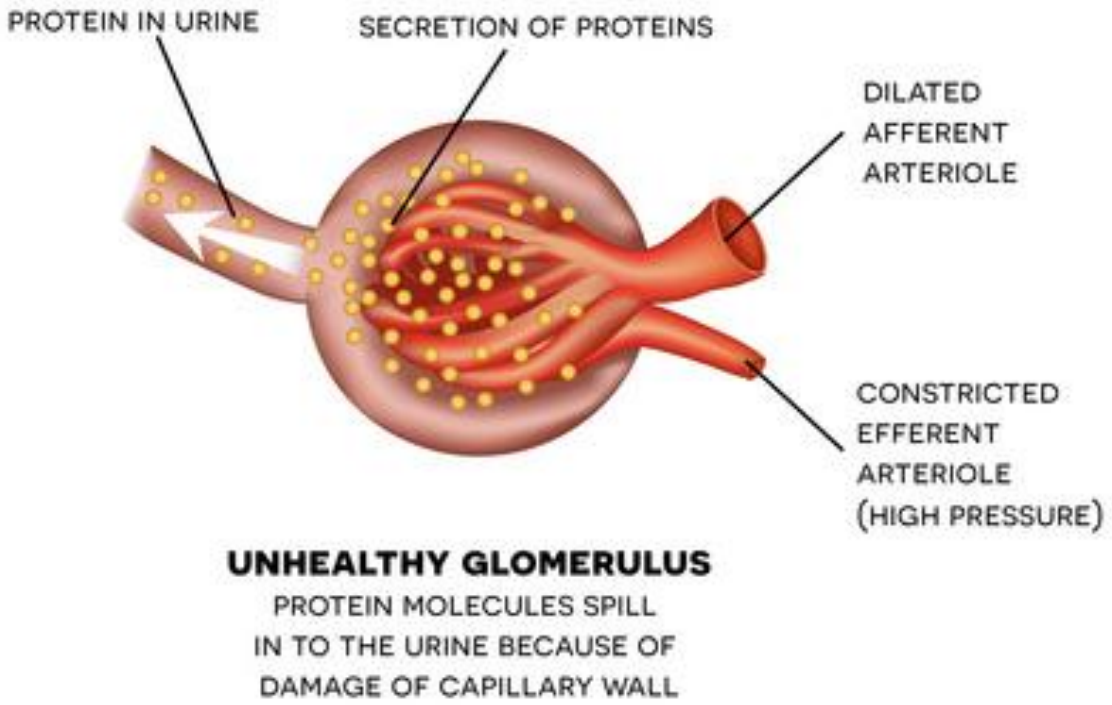
What Happens with DKD?



Nephrology. 2022; 10(1): 102-113

Pathophysiology of DKD





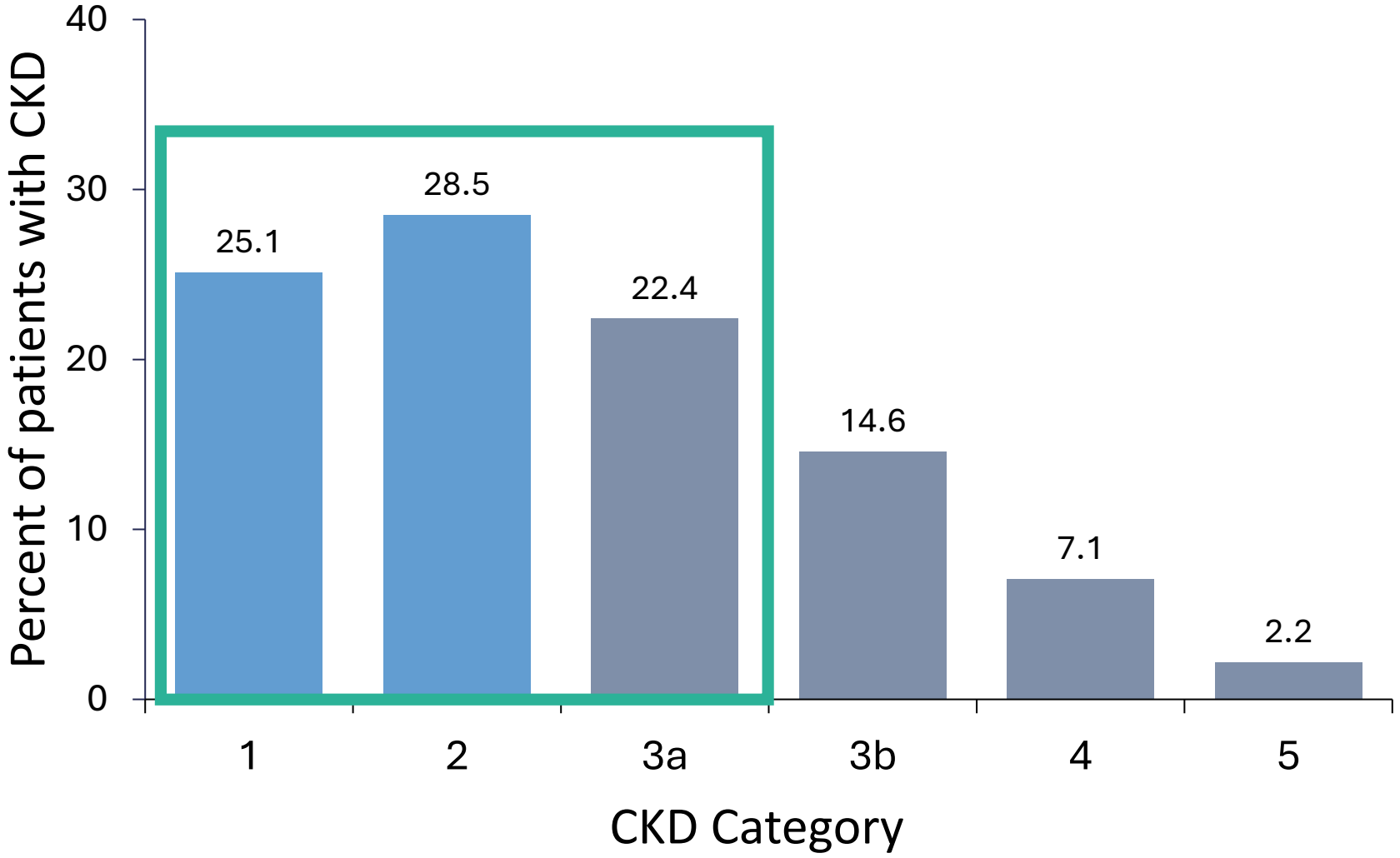
Nephrology. 2022; 10(1): 102-113

Most people do not experience symptoms until almost 90% of their kidney function is lost

SILENT Disease

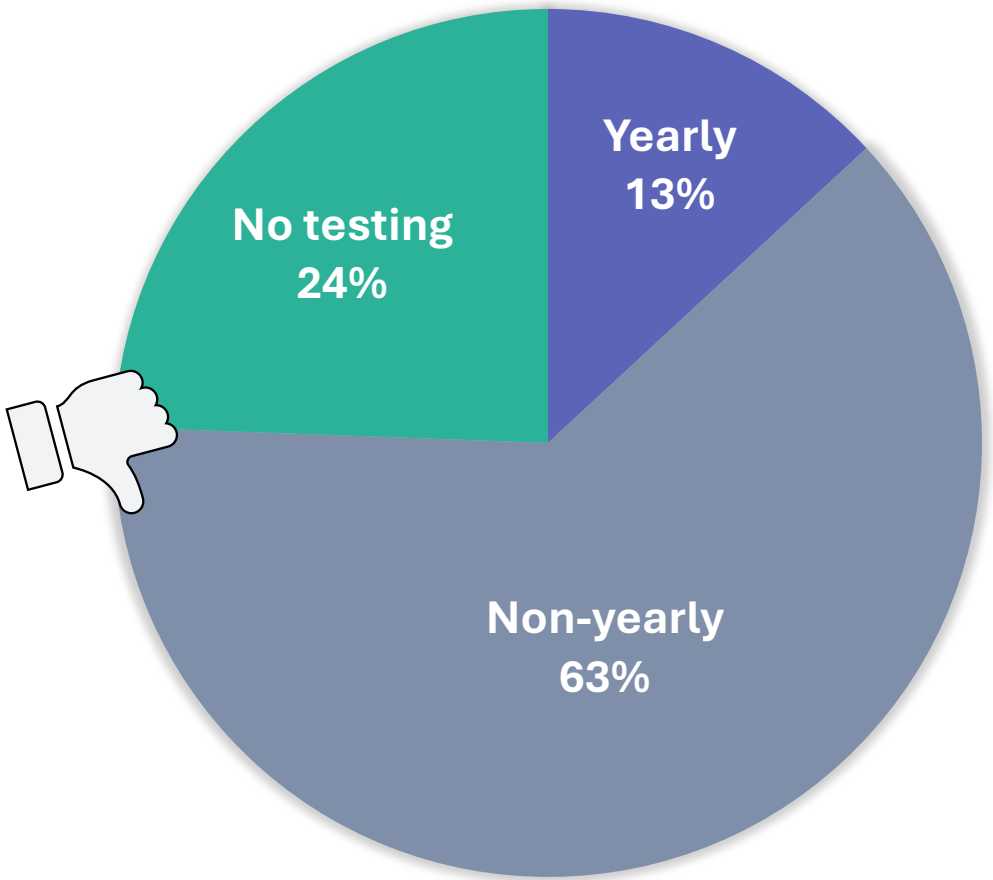
https://kidney.ca/KFOC/media/images/PDFs/Facing-the-Facts-2023-HIghlights-from-the-Annual-Statistics-on-Organ-Donation.pdf;
https://kidney.ca/KFOC/media/images/PDFs/Why-Kidney-Disease-Should-Matter-to-You_2025.pdf

Opportunity to Intervene Early



Clin Ther. 2021 Sept;4(3): 1558-1573

eGFR & UACR Testing Yearly for 5 Years: A Canadian Study



Can J Diabetes. 2024: 48(8): 487-492.

Screening and Detection

Yearly

Starting from T2D diagnosis

eGFR

Measures kidney function

UACR

Measures kidney damage

Can J Diabetes. 2025; 49(2): 73-86; Kidney Int. 2022; 102: S1-S127; Diabetes Care. 2024; 47: S219-S230.

Thresholds for DKD

Need **2 of 3** positive UACR **over 3 months**

UACR ≥ 2 mg/mmol

±

eGFR < 60 mL/min/1.73m^2

for at least 3 months

Kidney Int. 2024:105(4S):S117-S314; Can J Diabetes. 2025; 49(2): 73-86

Be Aware

Potential Causes of Transient Albuminuria

- Recent major exercise
- Urinary tract infection
- Severe febrile illness
- Decompensated heart failure
- Menstruation
- Acute severe elevation in blood glucose
- Acute severe elevation in BP

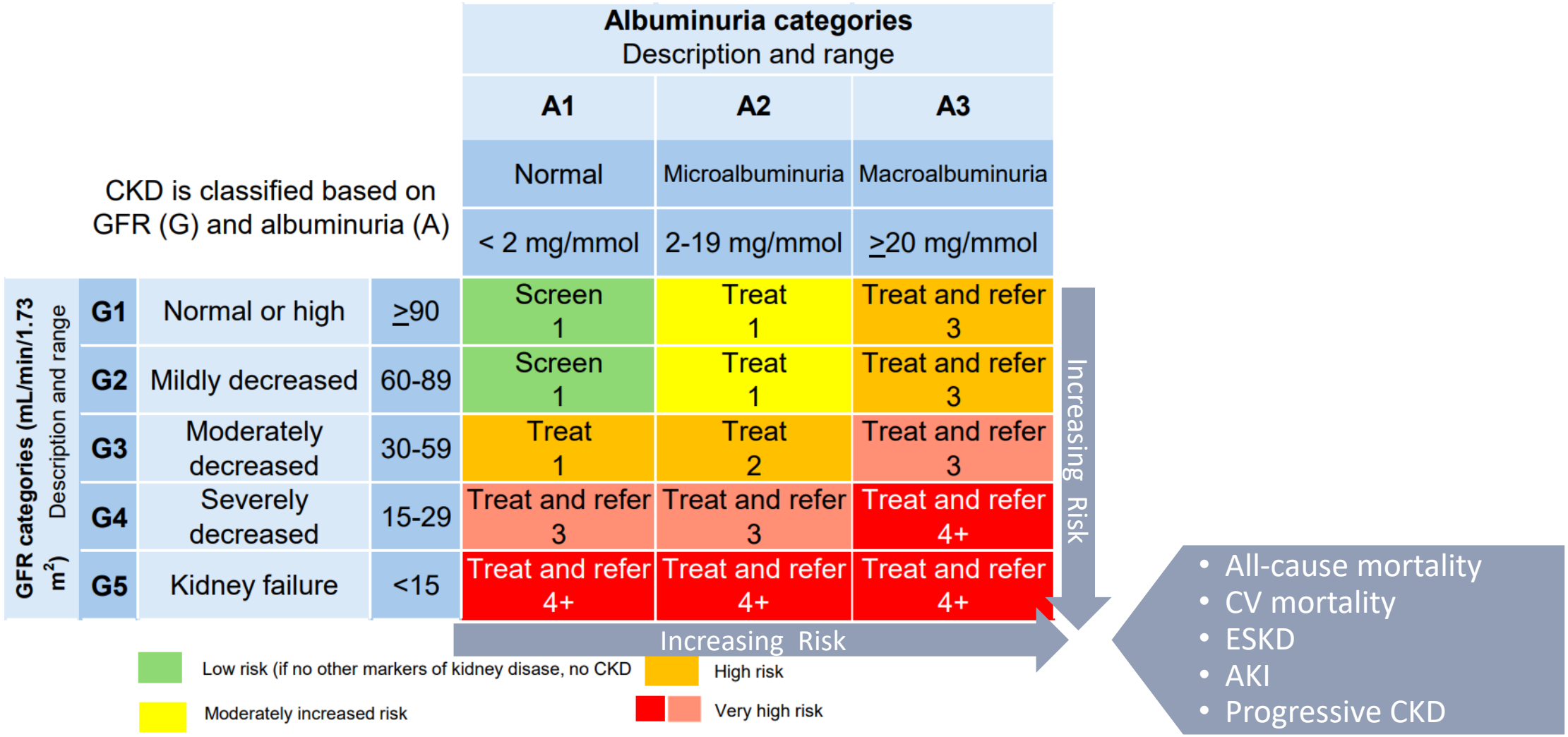
Can J Diabetes. 2025; 49(2): 73-86

Categories of DKD

Categories	Urine Dipstick	UACR (mg/mmol)		24h-albumin (mg/day)
		Diabetes Canada	KDIGO	
A1 (normal)	Negative	< 2	< 3	< 30
A2 (microalbuminuria)	Negative	2 – 20	3 – 30	30 – 300
A3 (overt albuminuria)	Positive	> 20	> 30	> 300

Can J Diabetes. 2025; 49(2): 73-86; Kidney Int. 2022; 102: S1-S127; Diabetes Care. 2024; 47: S219-S230.

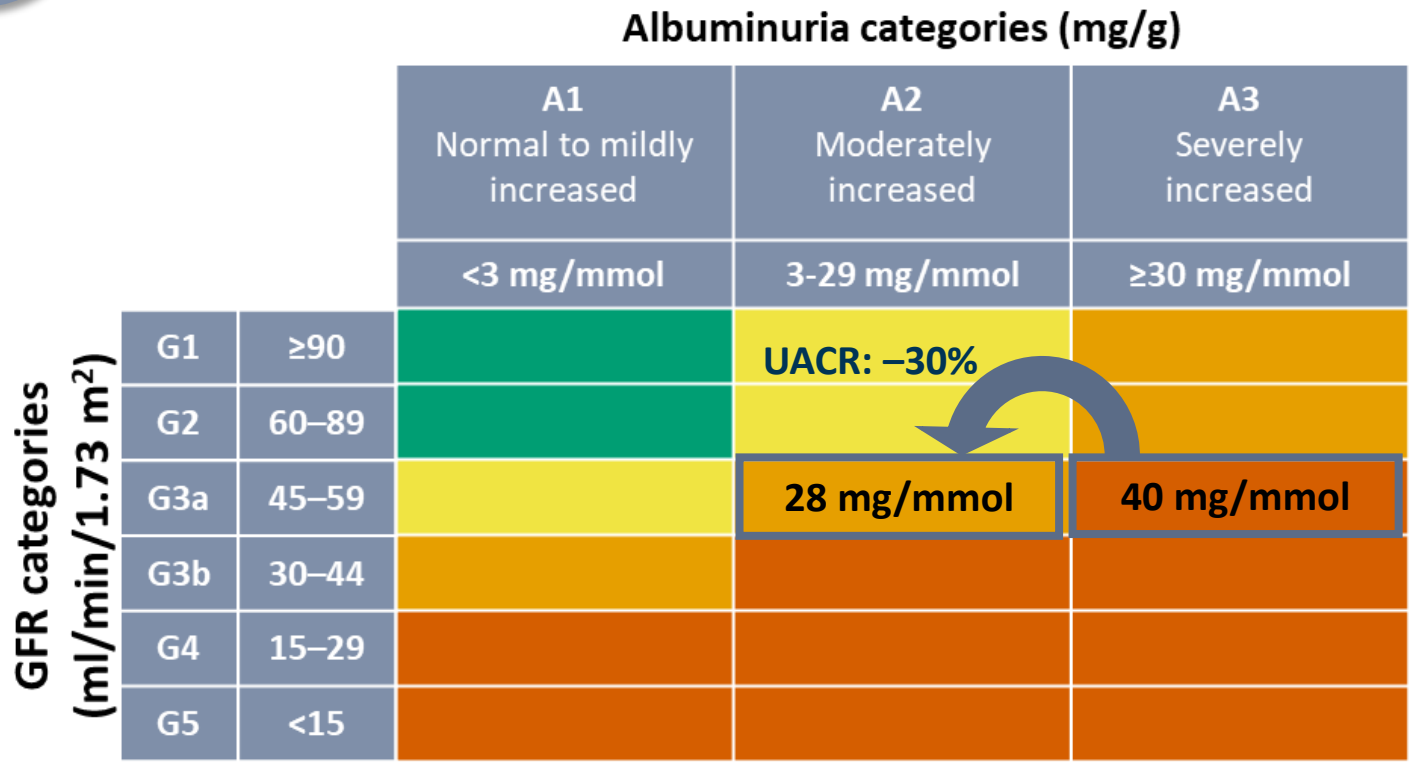
Risk of CKD Progression and Outcomes



Can J Diabetes. 2025; 49(2): 73-86

UACR: Treatment Target to Reduce the Risk of CKD Progression

ADA recommendation: In people with CKD who have ≥30 mg/mmol urinary albumin, a reduction of 30% or greater is recommended to slow CKD progression



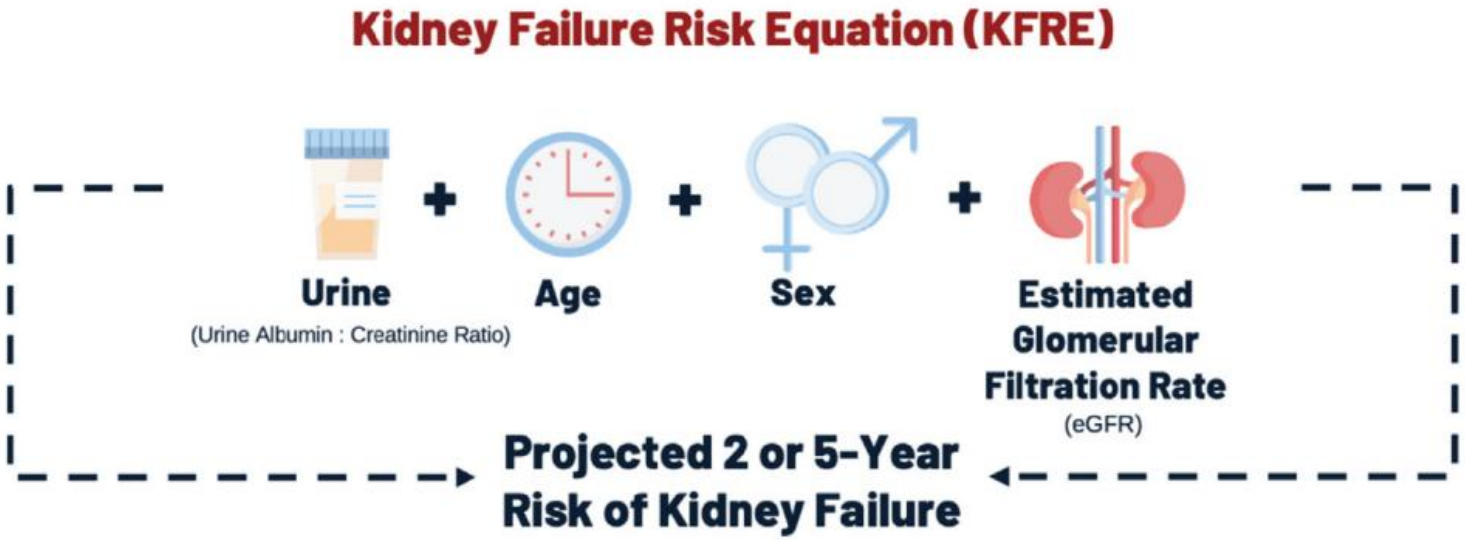
A meta-analysis of clinical trials suggests a **≥30% reduction in UACR is associated with a 27% risk reduction** of the **composite kidney outcome**

Kidney Int. 2022; 102: S1-S127; Diabetes Care. 2024; 47: S219-S230; Lancet Diabetes Endocrinol 2019;7:128–139

What does UACR and eGFR tell us?

Developed by K.Halliday, PharmD class 2026

Kidney Failure Risk Equation (KFRE) Predicts Risk of ESKD over 5 years: Categories 3-5



KFRE Score	Threshold for referral in NS
≥ 5% at 5 year	Refer

https://kidneyfailurerisk.com; JAMA 2011; 305(15):1553-9; Can J Diabetes. 2025; 49(2): 73-86

Criteria for Nephrology Referral

RECOMMENDED REASON FOR REFERRAL (Check all that apply and attach results to referral) **N.B. SEE BACK OF FORM FOR TRIAGE CRITERIA**	
☐ Rapidly declining eGFR by > 20 % over days to weeks	☐ Hereditary Kidney Disease (e.g. Polycystic kidney Disease)
☐ eGFR < 30 mL/min/1.73m^2 (X 2 results)	☐ Potassium or acid-base disorders
☐ eGFR 30-60 **AND** eGFR decline ≥ 10 ml/min/1.73m^2 in 1 year	☐ Pregnancy & CKD
☐ ACR > 60 mg/mmol in non-diabetic (x2 results)	☐ Nephrolithiasis + CKD (after Urology evaluation)
☐ ACR > 30 mg/mmol in non-diabetic, age < 70 (X 2 results)	☐ Persistent isolated hematuria ACR < 3mg/mmol + eGFR ≥ 60 (X 2 results) (after Urology evaluation)
☐ Suspected glomerulonephritis (hematuria + ACR > 3 mg/mmol ± eGFR decline)	
☐ Kidney Failure Risk > 5 % at 5 yrs: Use Kidney Failure Risk Equation (KFRE) to estimate risk Go to: http://kidneyfailurerisk.com or Smartphone App QxMD/Nephrology/Chronic Kidney Disease	

Case Vignette: KF

Demographics	Medical History	Labs	Medications
50-year-old female H: 5’5; W: 110 lbs	T2D HTN (BP 128/78 mmHg)	A1C = 8.2% eGFR = 50mL/min/1.73m^2 UACR = 10 mg/mmol (2 of 3 > 2 mg/mmol)	Ramipril 10 mg daily Metformin 1000 mg BID Rosuvastatin 10 mg daily

Polling Question #1

Based on KF's UACR and eGFR, what is their risk for CKD progression?

a) Low risk
b) Moderately increased risk
c) High risk
d) Very high risk

Polling Question #2

Which of the following guideline-recommended pillars would you be comfortable recommending for KF?

a) SGLT2i
b) GLP1RA
c) Finerenone
d) All of the above

Polling Question #3

Which of the following have demonstrated significant cardiovascular and kidney protection in patients with CKD and T2D?

a) GLP1RA
b) Finerenone
c) SGLT2i
d) All of the above

KF's CKD Category

CKD is classified based on GFR (G) and albuminuria (A)

GFR categories (mL/min/1.73 m²) Description and range				Albuminuria categories Description and range		
				A1	**A2**	**A3**
				Normal	Microalbuminuria	Macroalbuminuria
				< 2 mg/mmol	2-19 mg/mmol	≥20 mg/mmol
	G1	Normal or high	≥90	Screen 1	Treat 1	Treat and refer 3
	G2	Mildly decreased	60-89	Screen 1	Treat 1	Treat and refer 3
	G3	Moderately decreased	30-59	Treat 1	Treat 2 ★	Treat and refer 3
	G4	Severely decreased	15-29	Treat and refer 3	Treat and refer 3	Treat and refer 4+
	G5	Kidney failure	<15	Treat and refer 4+	Treat and refer 4+	Treat and refer 4+

Low risk (if no other markers of kidney disase, no CKD

Moderately increased risk

High risk

Very high risk

Can J Diabetes. 2025; 49(2): 73-86.

KF’s Kidney Failure Risk

STAGE 3

MODERATE DECREASE IN FUNCTION

CKD STAGES | GLOMERULAR FILTRATION RATE

Patient risk of progression to kidney failure requiring dialysis or transplant:

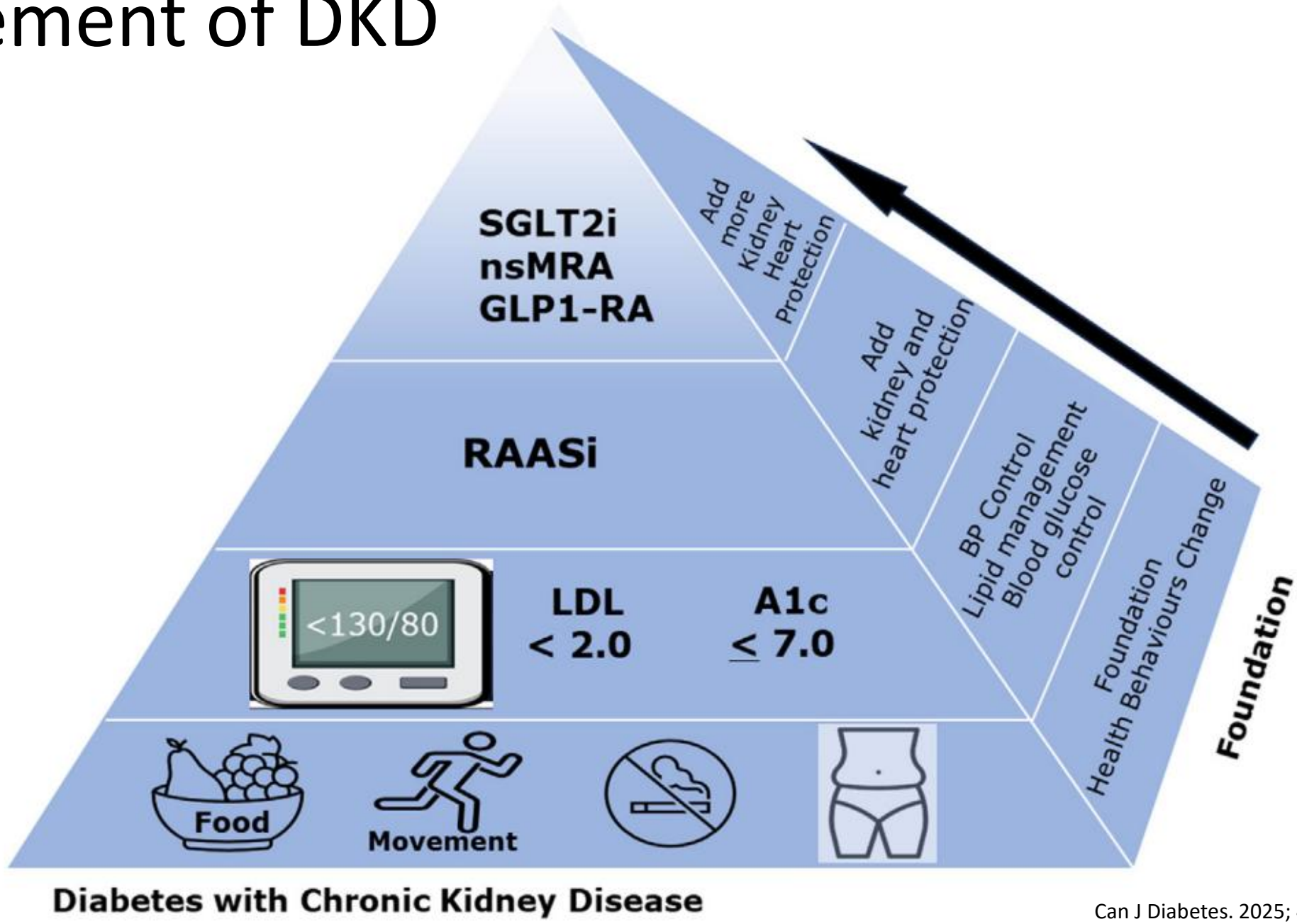
AT 2 YEARS	AT 5 YEARS
0.54 %	1.69 %

Risk thresholds used in health systems include:

- 3-5 % over 5 years for referral to a kidney doctor
- 10 % over 2 years for team based care (Kidney Doctor, Nurse, Dietician, Pharmacist)
- 20-40 % over 2 years for planning a transplant or fistula

https://kidneyfailurerisk.com/

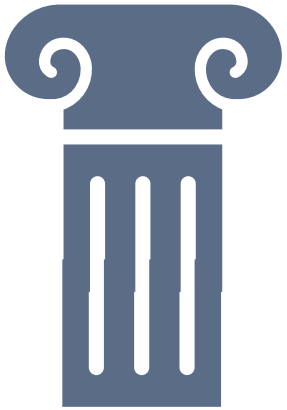
Management of DKD



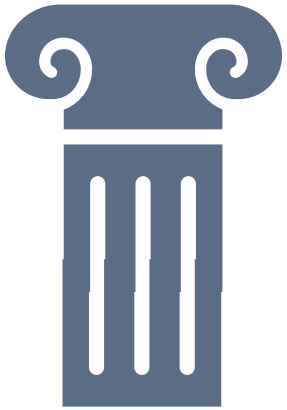
Can J Diabetes. 2025; 49(2): 73-86.

Pillars of DKD Management

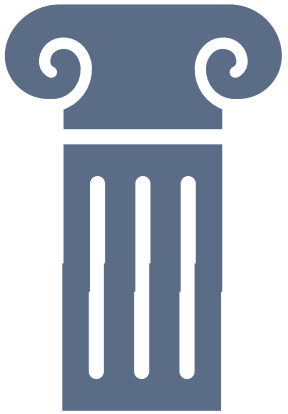
ACEi/ARB



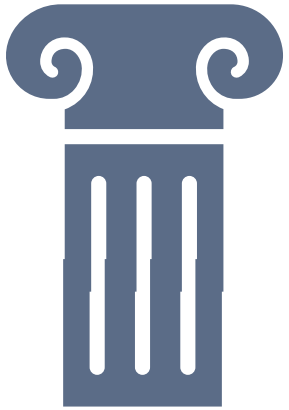
SGLT2i



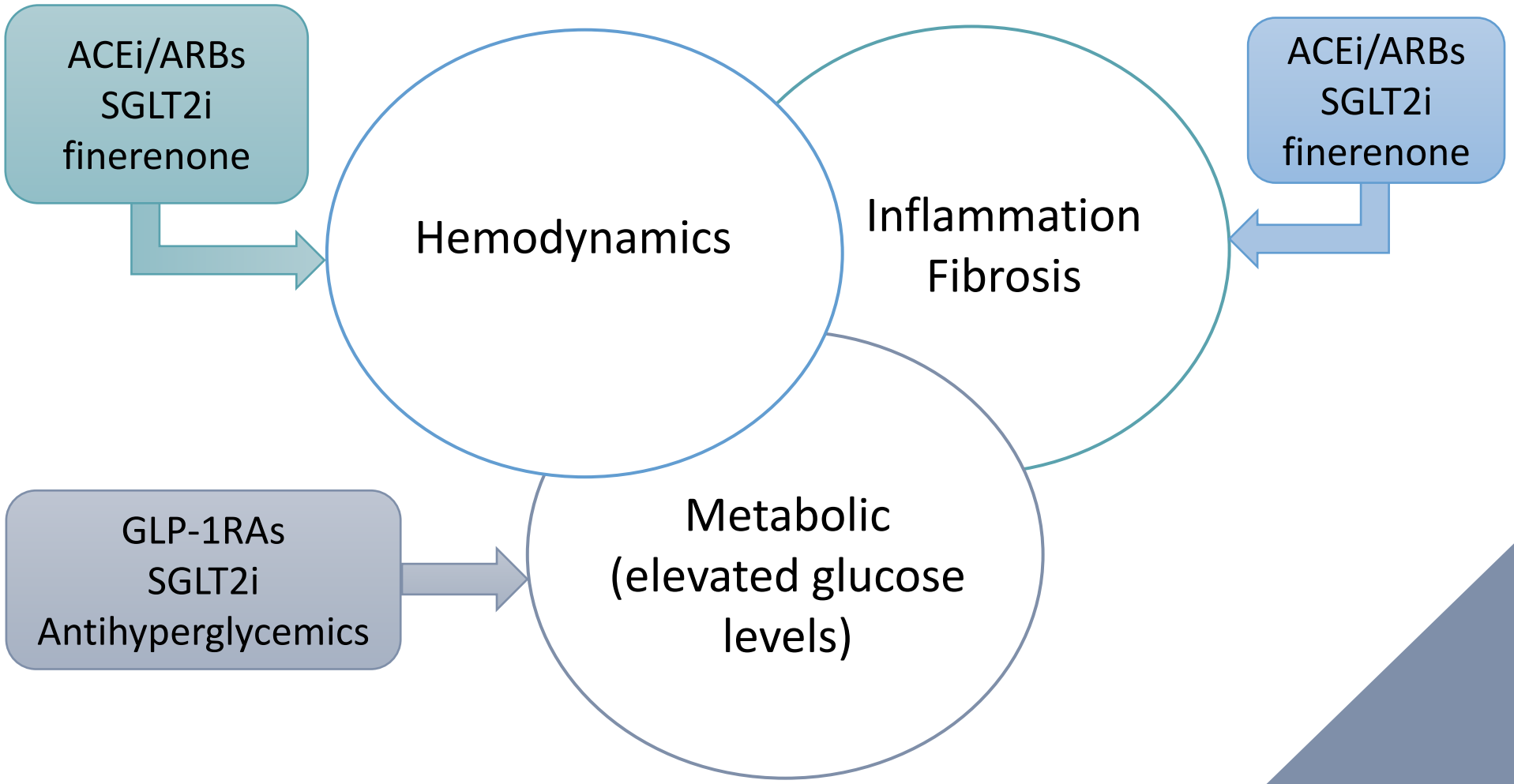
GLP1RA



Finerenone



Why multiple pillars of care? Drivers of CKD Progression



World Journal of Pharmaceutical and Life Sciences. 10(1): 119-127

Strategies to Promote Kidney and CV health

Involve patients and align on priorities

Optimize use of disease-modifying therapies

Target all drivers of disease progression

Evidence: ACEi or ARB

Trial	Albuminuria	Baseline renal function	2xCr, ESKD, Renal Death - # of events	RRR	NNT
IDNT (Irbesartan)	Median 1900 mg/d (1000 – 3800 mg/d)	Mean Cr: 148 µmol/L	644	20% (p = 0.006)	16
RENAAL (Losartan)	Median ACR: ~1250	Mean Cr: 168 µmol/L	686	16% (p = 0.02)	28
ACEi Collaborative Study Group (Captopril)	Mean proteinuria: 2500 mg/d	Mean Cr: 115 µmol/L	2xCr: 68 Death or ESKD: 65	43% (p = 0.007) 46%	11

N Engl J Med. 2001; 345: 851-60; N Engl J Med. 2001; 345: 861-69; N Engl J Med. 1993; 329: 1456-1462.

ACEi/ARB: Practical Tips

Initiate: if hypertension OR albuminuria

Use **maximally tolerated dose:**

The dose not associated with low BP OR hypotensive symptoms OR ↑K+ > 5.0 OR ↑ SCr >30% from baseline

Note: lower starting doses may be needed in older adults or if BP is already at target

Avoid: initiation or dose titration if K+ > 5 mmol/L, ACEi + ARB, pregnancy or if planning pregnancy in short term

ACEi/ARB: Practical Tips

Check

- SCr and K+ in 1-2 weeks post initiation/dose increases
  - If SCr > 30%: stop and consult
  - If K+ > 5.0 mmol/L: stop/reduce dose and consult

Monitor

- BP as needed (daily – weekly) and educate on hypotensive symptoms

Adverse Effects

- Dry cough (ACEi >ARB), hyperkalemia, hypotension, angioedema

Evidence: SGLT2i

Study, population	CKD Entry Criteria	Primary Composite Endpoint & Results
CREDENCE Canagliflozin in patients with T2D and CKD	eGFR: 30 to <90 mL/min/1.73 m^2 AND UACR: 33.9 to 565 mg/mmol	ESKD (dialysis, transplantation, or a sustained eGFR <15 mL/min/1.73 m^2), 2xSCr, or death from renal or CV causes **Canagliflozin vs. Pb:** RRR 30%**;** HR: 0.70 (95.02% CI, 0.59, 0.82); *p*=0.00001 **NNT:** 22/3.5 years
DAPA-CKD Dapagliflozin in patients with CKD +/- T2D	eGFR: 25 to 75 mL/min/1.73 m^2 AND UACR: 22.6 to 565 mg/mmol	Sustained ≥50% eGFR Decline, ESKD (need for maintenance dialysis for ≥28 days and renal transplantation or sustained eGFR <15mL/min/1.73m^2 for ≥28 days, renal or CV death **Dapagliflozin vs. Pb:** RRR 39%; HR 0.61 (95% CI, 0.51-0.72); *p*<0.0001 **NNT:** 19/2.4 years
EMPA-KIDNEY Empagliflozin in patients with CKD +/- T2D	eGFR 20 to <45 mL/min/1.73 m^2 OR eGFR 45 to <90 mL/min/1.73 m^2 AND UACR ≥22.6 mg/mmol	Progression of kidney disease (ESKD, sustained decrease in eGFR to <10 mL/min/1.73 m2, sustained decrease in eGFR of ≥40% from baseline, or death from renal causes) or death from CV causes **Empagliflozin vs. Pb:** RRR 28%; HR 0.72 (95% CI, 0.64-0.82); *p*<0.001 **NNT:** 26/2 years

N Engl J Med 2019;380(24):2295-2306; N Engl J Med 2020;383(15):1436-1446; N Engl J Med. 2023; 388(2):117-127

SGLT2i Cardiorenal Benefits: Meta-Analysis
with and without diabetes

↓ **37%** risk of kidney disease progression
RR 0.67, CI 0.58–0.69

↓ **23%** risk of acute kidney injury
RR 0.67, CI 0.58–0.69)

↓ **23%** risk of CV death or HHF
RR 0.77, CI 0.74–0.81

A1C[†]
-0.69%

Body weight[†]
-2.1 kg

Systolic BP
-3.9 mmHg

[†]the A1C lowering and weight loss effect of SGLT2i are reduced at lower eGFR levels

Lancet. 2022;400(10365):1788-1801

SGLT2i: Practical Tips

Cardiorenal Daily Doses:
- Empagliflozin 10 mg
- Dapagliflozin 10 mg
- Canagliflozin 100 mg

Ensure patients are well **hydrated** prior to initiation

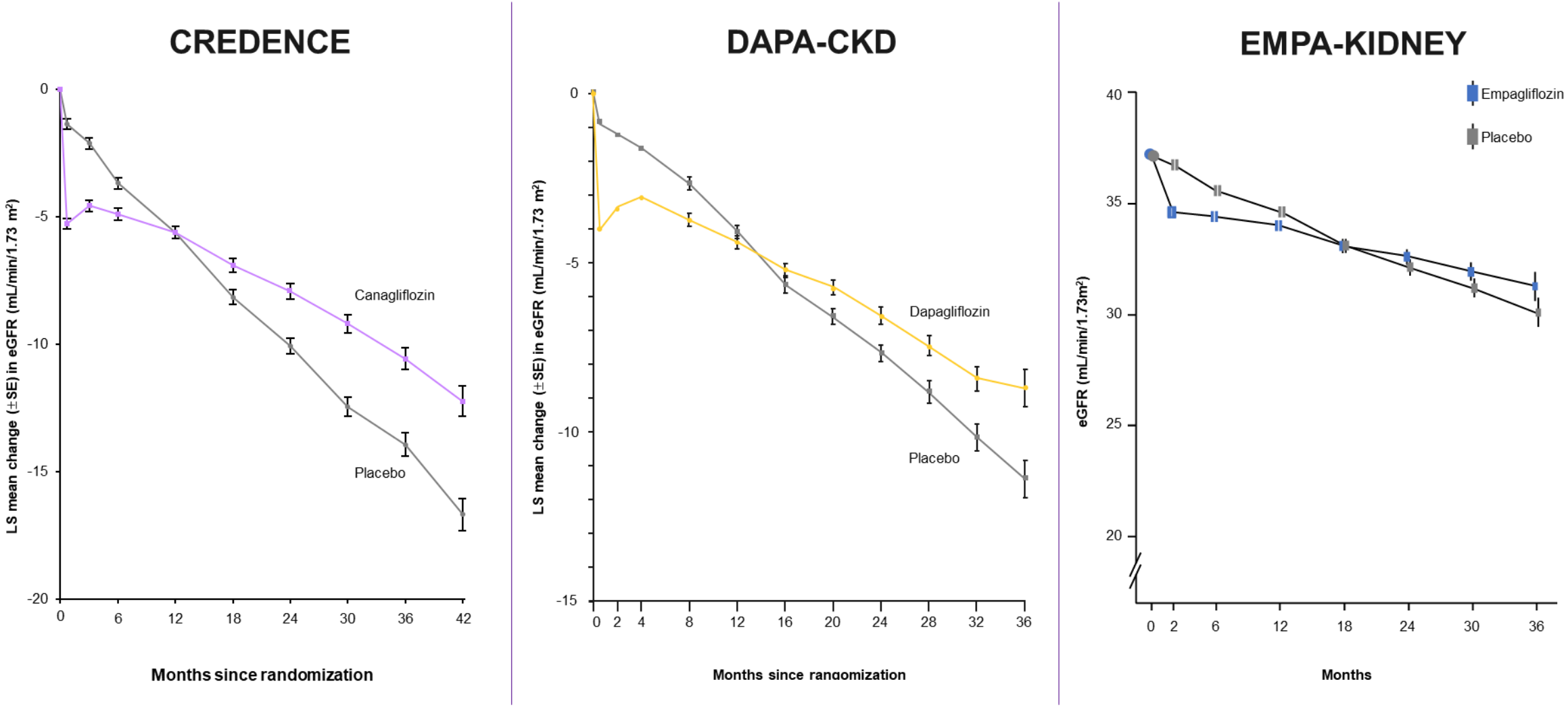
Initiate: If eGFR ≥ 20 mL/min/1.73m^2
Continue: to dialysis or kidney transplantation

- Routine eGFR and lytes after the initiation are recommended **only in cases where there is clinical concern** about volume status (BP <120/70 mmHg, s/s of volume depletion, high-dose diuretics, elderly, eGFR < 45 mL/min/1.73 m^2).
- If eGFR↑ 30%: Stop and refer
- Expect eGFR dip by 3-4 mL/min/1.73m^2 in first 2 weeks
- UACR ↓ weeks-months

- Avoid: history of DKA, prolonged fasting
- Provide sick day medication guidance (SADMANs)
- Risks: UTIs, genital mycotic infections, volume depletion/hypotension, hypoglycemia (rare), DKA (rare)

Can J Kid Health Dis. 2023; 10: 1-22

Expected eGFR Dip Post-Initiation



N Engl J Med. 2019 Jun 13;380(24):2295-2306; N Engl J Med. 2020; 383:1436-1446; N Engl J Med. 2023;388(2):117-127.

Evidence: Semaglutide FLOW Trial (T2D)

eGFR 50 – 75 mL/min/1.73m2 and UACR > 33.9 to < 565 mg/mmol
OR eGFR 25 to < 50 mL/min/1.73m2 and UACR > 11.3 to < 565 mg/mmol)

Primary Outcome

24%

Major kidney disease events:
kidney failure, sustained ≥ 50% reduction in eGFR from baseline or death from kidney-related or cardiovascular causes
HR 0.76 (95% CI 0.66 – 0.94)
NNT = 20/3 yrs

Secondary Outcome

18%

Risk of MACE
HR 0.82 (95% CI 0.68 – 0.98)
NNT = 45/3 yrs

20%

Risk of death from any cause
HR 0.8 (95% CI 0.67 – 0.95)
NNT = 39/3 yrs

1.16
mL/min/1.73 m²

Mean annual eGFR slope difference compared to Pb

N Eng J Med. 2024; 391(2): 109-121

GLP1-RA: Practical Tips

Initiate: if eGFR ≥ 15 mL/min/1.73m^2 and UACR ≥ 11 mg/mmol

Avoid: Pregnancy or breast feeding (discontinue in women ≤ 2 months prior to planned pregnancy), personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2, concurrent DPP4i

GLP1-RA: Practical Tips

Starting dose: Semaglutide

- 0.25 mg subcut. once weekly for 4 weeks, then 0.5 mg subcut. once weekly for 4 weeks, then 1 mg subcut. once weekly
- Note: additional glycemic control maximum 2 mg weekly

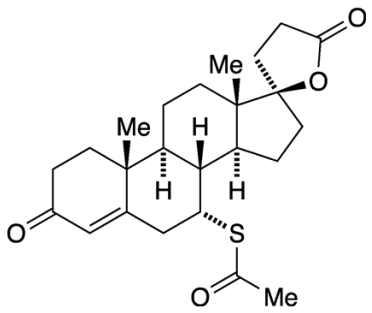
Monitoring

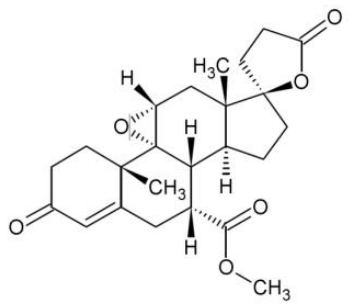
- GI upset (nausea) expected. Adjust titration schedule if significant
- Severe and ongoing pain in the stomach, seek care (possible pancreatitis)

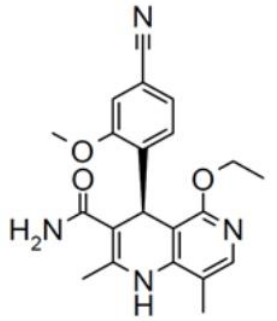
Additional Considerations

- Consider ↓ dose of insulin secretagogues (sulfonylureas) or insulin (by 20%)

Finerenone: *nonsteroidal* MRA







	Spironolactone	Eplerenone	Finerenone
Mineralocorticoid Receptor selectivity	+	++	+++
Half-life	> 20 h	4-6 h	2-3 h
Tissue Distribution			
Active metabolites	++	-	-
Sexual side effects	++	+	-
Effect on BP	+++	++	+
Indication for HTN	Yes	Yes	No
Indication for HFrEF	Yes	Yes	No

Br J Pharmacol. 2021 Nov 22; Handb Exp Pharmacol 2017;243:271–305;Aldactone®(spironolactone) Product Monograph. 2022. Pfizer Canada; Inspra® (eplerenone) Product Monograph. 2023. Pfizer Canada;Kerendia® (finerenone) monograph. 2022. Bayer Inc

Evidence: Finerenone

	FIDELIO-DKD	FIGARO-DKD
Patients	Predominantly stage 3–4 CKD with severely increased albuminuria	Predominantly stage 1–2 CKD with moderately or severely increased albuminuria
Primary endpoint	↓ CKD progression by 18% (HR=0.82; CI 0.73–0.93) NNT = 29	↓ CV mortality and morbidity by 13% (HR=0.87; 95% CI 0.76–0.98) NNT = 47
Secondary endpoint	↓ CV mortality and morbidity by 14% (HR=0.86; CI 0.75–0.99) NNT = 55	↓ CKD progression by 13% (non-statistically significant) (HR=0.87; 95% CI 0.76–1.01)
Safety	Both trials showed that finerenone was generally well tolerated and that the increased incidence of hyperkalemia had a minimal clinical impact in the studies	

N Engl J Med 2020;383:2219–2229; N Engl J Med. 2021 Dec 9;385(24):2252-2263.

FIDELITY: A Pooled Analysis of FIDELO & FIGARO

Participants: N = 13,025

T2D and CKD (eGFR > 25 mL/min/1.73 m2) with moderately – severe albuminuria, serum K+ < 4.8 mmol/L and maximum tolerated ACEi/ARB

Clinical Endpoints	HR (95% CI)	NNT
Kidney Composite (time to kidney failure, sustained ≥ 57% decrease in eGFR from baseline ≥ 4 weeks, or death from kidney causes)	0.77 (0.67-0.88)	**60/3 yrs**
CV Composite (time to death from CV causes, non-fatal MI, nonfatal stroke or hospitalization for HF)	0.86 (0.78-0.95)	**46/3 yrs**

European Heart J. 2022; 43: 474-484; Can Pharm J. 2024; 157(4): 174-180

FIDELITY: A Pooled Analysis of FIDELO & FIGARO

No difference in hypoglycemia
Finerenone: 5.2%
Placebo: 5.8%

Any Hyperkalemia
Finerenone: 14%
Placebo: 6.9%

No gynecomastia
Finerenone: 0.10%
Placebo: 0.20%

Hyperkalemia leading to discontinuation
Finerenone: 1.7%
Placebo: 0.6%

Systolic BP
Finerenone: -3.2 mmHg
Placebo: +0.5 mmHg

European Heart Journal. 2022; 43: 474-484

Finerenone: Practical Tips

Initiate: If eGFR ≥ 25 mL/min/1.73m^2, K+ ≤ 4.8 mmol/L AND UACR ≥ 3 mg/mmol despite maximally tolerated ACEi or ARB

1

Serum K+ (mmol/L)	Recommendation
≤ 4.8	Initiate
> 4.8 to 5.0	Consider with additional K+ monitoring within first 4 weeks based on patient characteristics and K+ levels
> 5.0	Not recommended

Avoid: if on another MRA (spironolactone, eplerenone), CHF NYHA 11-IV, grapefruit, strong CYP3A4 inhibitors (e.g., ketoconazole, ritonavir, clarithromycin)

2 eGFR (mL/min/1.73 m²)	Initial Dose	
> 60	20 mg once daily	
≥ 25 to < 60	10 mg once daily	
< 25	Not recommended	
At 4 weeks: K+ (mmol/L) and reassess periodically*	3 Dose Adjustment Recommendation	
	If initial Dose: 10 mg	**If initial Dose: 20 mg**
≤ 4.8	↑20 mg daily If eGFR has not ↓ >30% from prior measurement	Maintain 20 mg daily
> 4.8 to 5.5	Maintain Dose	
> 5.5	Withhold Restart at 10 mg daily when K+ ≤ 5.0 mmol/L	

*based on patient characteristics and prior K+ values

Note: Discontinue eGFR < 15 ml/min/1.73m2

Finerenone: Practical Tips

Check

- Order SCr and K+ 4 weeks after initiation, re-start or dose titration, then every 2-4 months
- May cause eGFR dip 3-3.5 mL/min/1.73m^2 over first 4 months

Adverse Effects

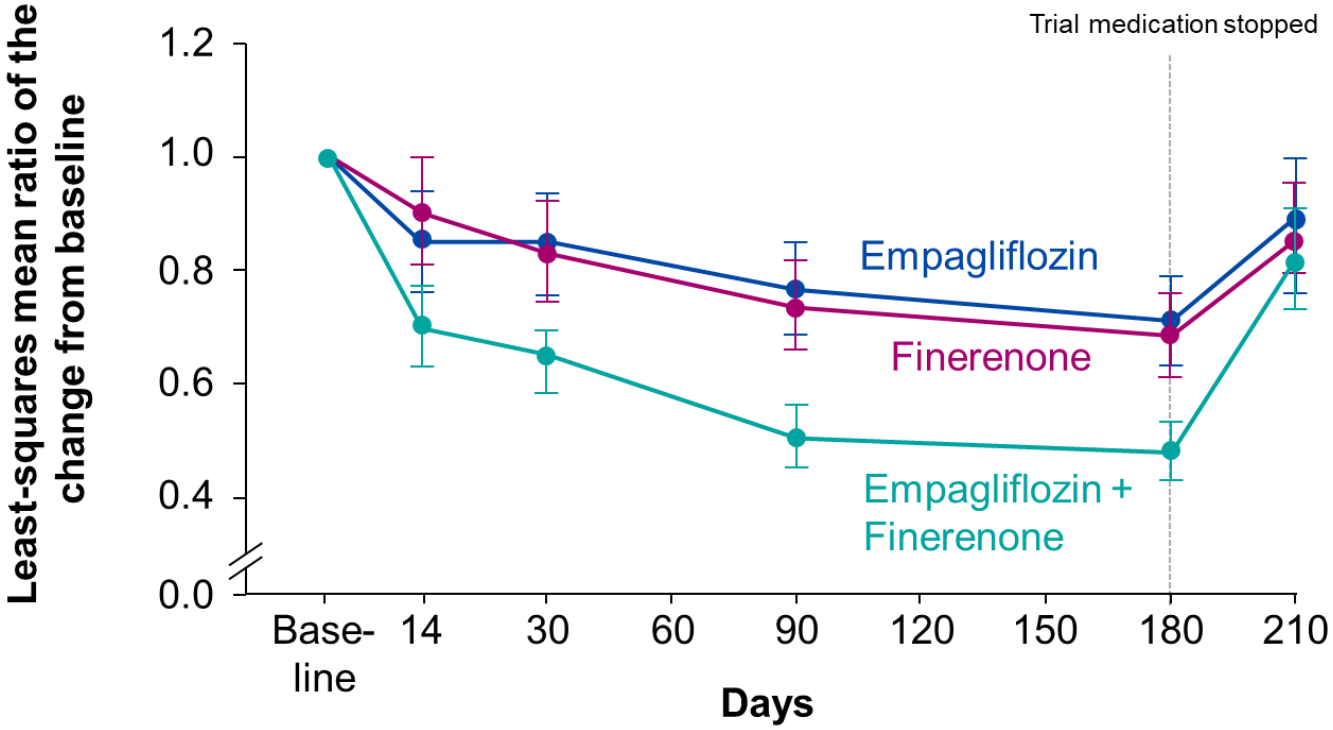
- hyperkalemia, hypotension (rare, mean ↓ systolic BP 3 mmHg)

Finerenone + Empagliflozin: CONFIDENCE Trial

Participants:
T2D, eGFR 30 – 90 mL/min/1.73m^2, UACR 34-565 mg/mmol, max tolerated dose ACEi/ARB

	Change in UACR from baseline at 180 days*
Empagliflozin	0.71 (32%)
Finerenone	0.68 (29%)
Empagliflozin + Finerenone	0.48 (52%)

*Least-Squares Mean Ratio



N Engl J Med. 2025 Jun 5. DOI: 10.1056/NEJMoa2410659

Finerenone + Empagliflozin: CONFIDENCE Trial

	Hyperkalemia	> 30% eGFR drop at day 30
Empagliflozin	3.8%	1.1%
Finerenone	11.4%	3.8%
Empagliflozin + Finerenone	9.3%	6.3%

Take Home Point:
Combination therapy results in a greater reduction in UACR than either agent alone with a lower incidence of hyperkalemia

N Engl J Med. 2025 Jun 5. DOI: 10.1056/NEJMoa2410659

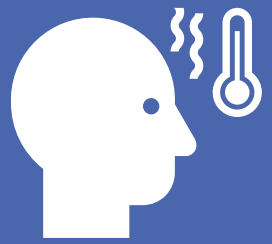
Other Patient Considerations and Priorities

Consideration	SGLT2i	Finerenone	GLP1-RA
Weight loss	+	0	++
Avoidance of hyperkalemia	+	-	0
Glycemic control	+	0	++
Avoidance of genital infections	-	0	0
Avoidance of injections	+	+	-
NS Pharmacare Coverage	Dapa (SFD) Cana (E), Empa (E)	E	E

Can J Diabetes. 2025; 49(2): 73-86; Nova Scotia Formulary. 2011 Jul [cited 2025 Jul 25]. Available from: https://novascotia.ca/dhw/pharmacare/documents/formulary.pdf .

Sick Day Medication Guidance

Sick



Identifies dehydration (vomiting, diarrhea)

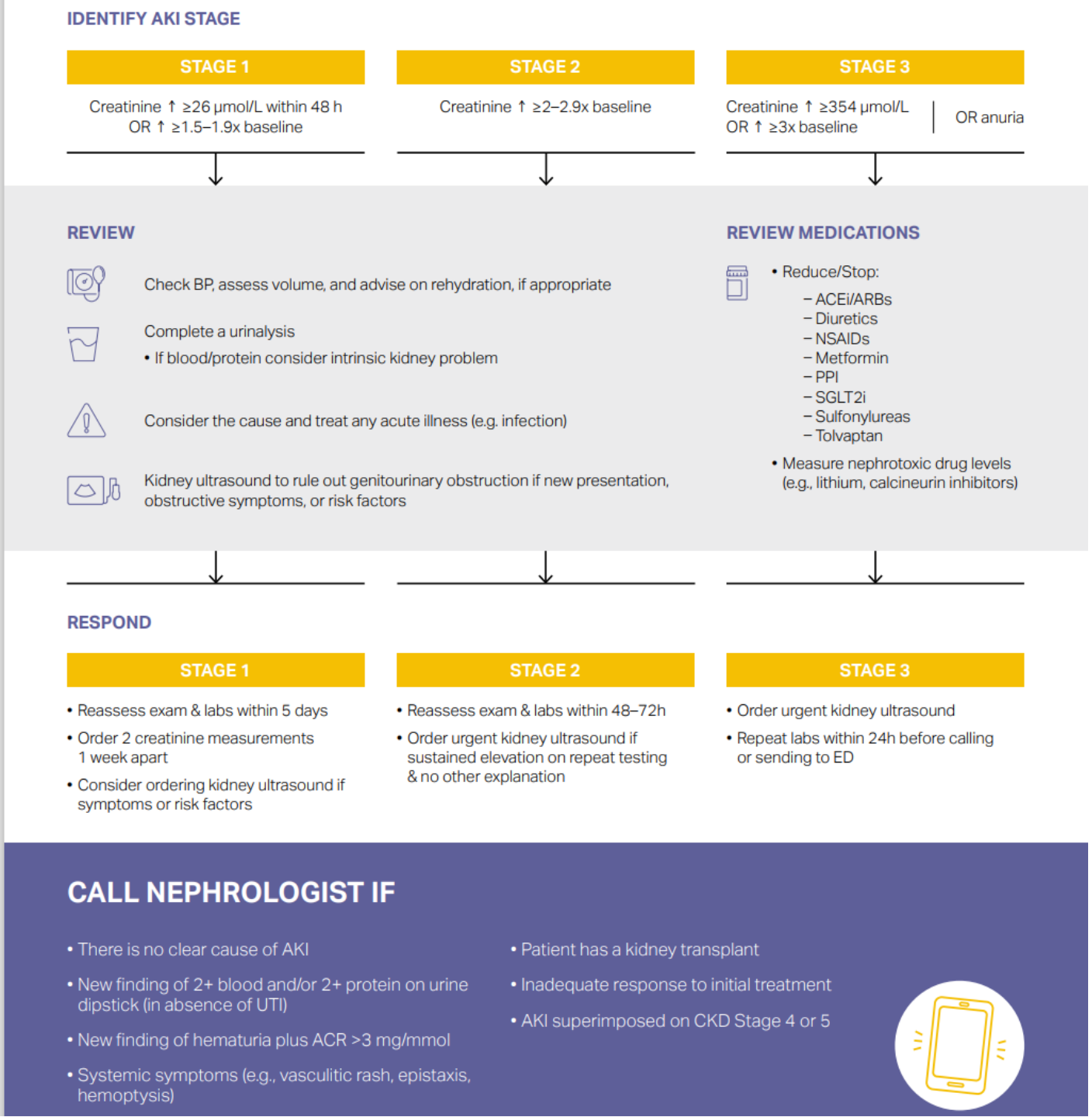
Recalls or retrieves list of medication to stop

- **S**ulfonylureas
- **A**CE inhibitors
- **D**iuretics
- **M**etformin
- **A**RBs
- **N**SAIDs
- **S**GLT2s

Recovers and resumes medication

https://www.diabetes.ca/ ; Am J Kidney Dis. 2023;81(5):564-574; Can Pharm J (Ott). 2024;157(4):174-180.

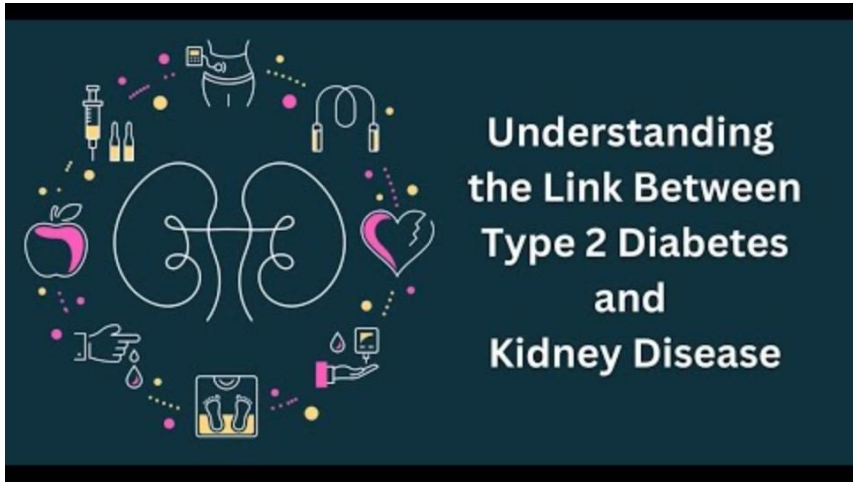
AKI: Referral and Management Guide



Resources: Patients

Diabetes.ca

Kidney.ca



Resources: Pharmacists

Diabetes.ca

29 Chronic Kidney Disease in Diabetes 2025 UPDATE
Chronic Kidney Disease in Diabetes 2018 ARCHIVED

KDIGO.com

KDIGO-Diabetes in CKD (2022)
KDIGO- CKD Evaluation and Management (2024)
ADA and KDIGO Consensus (2022)

CONSIDERATIONS FOR NOVA SCOTIA PHARMACISTS MANAGING T2D IN CKD

DID YOU KNOW THAT...

- 11 MILLION CANADIANS LIVE WITH DIABETES OR PREDIABETES
- DIABETES IS THE LEADING CAUSE OF KIDNEY DISEASE
- DIABETES CONTRIBUTES TO 38% OF KIDNEY FAILURE REQUIRING DIALYSIS

1 IN 3 PATIENTS WITH DIABETES HAVE CKD

PEOPLE WITH DIABETES ARE OVER 12 TIMES MORE LIKELY TO BE HOSPITALIZED WITH END-STAGE KIDNEY DISEASE

HAVING KIDNEY DISEASE INCREASES THE RISK FOR CARDIOVASCULAR DISEASE

WHEN TO SCREEN FOR CKD?

YEARLY STARTING AT DIAGNOSIS OF T2D

EARLY DETECTION & MANAGEMENT OF CKD CAN REDUCE PROGRESSION

HOW TO SCREEN FOR CKD?

BLOOD TEST: Measures SCr to calculate an eGFR to assess kidney function

+

URINE TEST: Measures urine ACR to assess level of kidney damage

*first morning void preferred

THRESHOLDS FOR CKD

eGFR < 60 mL/min/1.73m² ≥ 3 months **AND/OR** 2 urine ACR ≥ 3 mg/mmol ≥ 3 months

Consult NP/MD to refer to nephrology if eGFR < 30 mL/min/1.73m²

(https://cdn.dal.ca/content/dam/dalhousie/pdf/faculty/medicine/departments/department-sites/medicine/patient-care/Nephrology-Referral-Form-approved.pdf)

CKD STAGES, RISK OF CKD PROGRESSION, AND FREQUENCY OF MONITORING

LOW RISK
MODERATE RISK
HIGH RISK
VERY HIGH RISK

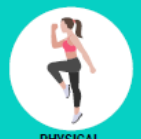
The numbers in each box indicate the recommended frequency of monitoring (number of times per year)

eGFR categories (mL/min/1.73m²)				Persistent albuminuria categories: A1 Normal to mildly increased <3 mg/mmol	A2 Moderately increased 3-30 mg/mmol	A3 Severely increased >30 mg/mmol
	G1	Normal or high	≥90	1	1	3
	G2	Mildly decreased	60–89	1	1	3
	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+

FIND OUT YOUR PATIENT'S RISK OF KIDNEY FAILURE: The Kidney Failure Risk Calculator (https://kidneyfailurerisk.com) is an online tool that calculates risk of kidney Failure in CKD stages 3 -5 based on patient-specific factors

OVERVIEW OF THE MANAGEMENT OF T2D IN CKD

LIFESTYLE



PHYSICAL ACTIVITY | WEIGHT MANAGEMENT | HEALTHY DIET | SMOKING CESSATION

Patient Information Booklet: https://kidney.ca/CMSPages/GetFile.aspx?guid=3effab70-b678-43ad-a461-f879956a2265

GOALS

GLYCEMIC CONTROL | BLOOD PRESSURE CONTROL | LIPID MANAGEMENT

KIDNEY PROTECTIVE MEDICATIONS

- **ACEi** (e.g., lisinopril, perindopril, ramipril) or **ARB** (e.g., candesartan, irbesartan, losartan)
- **SGLT2i** (dapagliflozin, canagliflozin, empagliflozin)
- **GLP-1RA** (semaglutide)
- **NONSTEROIDAL MRA** (finerenone)

WHY MANAGE CKD?

- ↓CKD PROGRESSION
- ↓CVD RISK
- ↓ALL-CAUSE MORTALITY
- ↓CKD COMPLICATIONS

BENEFITS

- ↓PROGRESSION OF CKD
- ↓ALBUMINURIA
- ↓CV RISK

ACEI OR ARB

Use maximally tolerated dose of ACEi or ARB if hypertension or albuminuria.

CLINICAL PEARLS

- Use **maximally tolerated dose** (one not associated with low BP OR hypotensive symptoms OR ↑K+ > 5.0 OR ↑SCr > 30% from baseline)
- Lower starting doses may be needed in older adults or if BP is already at target
- Order **SCr and lytes in 1-2 weeks** for **initiation** and **dose titration**
  - If ↑SCr > 30%: stop and consult (consider causes: NSAID, sick, AKI...)
  - If ↑K+ > 5.0 mmol/L: stop/reduce dose and consult (consider causes: diet, drugs, metabolic acidosis...)
- **Monitor BP as needed (daily to weekly)** and educate patients on hypotensive symptoms
- Educate patients on **SDMG** to ↓ risk of AKI
- ⚠**AVOID** initiation or dose titration if K+ > 5 mmol/L
- ⚠**AVOID** ACEi + ARB
- ⚠**AVOID** in pregnancy or if planning pregnancy in the short-term
- ⚠**RISKS:** Dry cough (ACEi >ARB), hyperkalemia, hypotension, angioedema

SGLT2i

Initiate if eGFR ≥ 20 mL/min/1.73m². Continue to dialysis or kidney transplantation.

CLINICAL PEARLS

- Cardiorenal daily doses: dapagliflozin 10 mg, empagliflozin 10 mg, canagliflozin 100 mg (no dose titration required)
- Assess and manage prior to starting SGLT2i:
  - Is A1C ≤7.0% and taking insulin or SU? → Consider ↓ insulin, and/or ↓ or stop SU
  - Is patient hypovolemic? → Consider changing diuretic dose
  - Is patient hypotensive? → Stop or ↓ diuretic or other BP medications (Prioritize maintaining ACEi or ARB if possible)
- Ensure patients hydrated before starting
- Order **SCr 4 weeks after initiation**. If SCr ↑30%: Stop and consult
- Expect an eGFR dip 3-4 mL/min/1.73m² within first 2 weeks (reflects kidney protection)
- ↓urine ACR seen in weeks to months
- Diminished glucose lowering at eGFR < 60 ml/min/1.73m²
- Educate patients on SDMG to ↓ risk of AKI
- ⚠**AVOID** if history of DKA
- ⚠**DO NOT** use if prolonged fasting
- ⚠**RISKS:** UTIs, genital mycotic infections, volume depletion/hypotension, hypoglycemia (rare), euglycemic DKA (rare)

GLP-1RA

Initiate if eGFR ≥ 15 mL/min/1.73m². Limited evidence for use on hemodialysis.

CLINICAL PEARLS

- Starting dose: semaglutide 0.25 mg subcut. once weekly for 4 weeks then 0.5 mg subcut weekly for 4 weeks then 1 mg subcut weekly thereafter. (Note: additional glycemic control maximum 2 mg weekly)
- Delays gastric empyting, GI upset (nausea) expected. Adjust titration schedule if side effects are significant. Consider eat more frequent low fat meals to ↓ GI upset
- When initiating, consider ↓ dose of insulin secretagogues (sulfonylureas) or insulin (by 20%)
- If severe and on going pain in the stomach, seek care right away (possible sign of pancreatitis)
- Store unused pens between 2 - 8 C, store pens in use below 30 C for up to 56 days
- ⚠**AVOID:** pregnancy or breast feeding. Discontinue in women at least 2 months before a planned pregnancy due to long washout period
- ⚠**AVOID:** personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2
- ⚠**AVOID:** concurrent DPP4i

FINERENONE

Initiate if eGFR ≥ 25 mL/min/1.73 m², $K^+ \leq 4.8$ mmol/L, and urine ACR ≥ 3 mg/mmol despite maximally tolerated ACEi or ARB (stop if $K^+ \geq 5.5$ mmol/L).

CLINICAL PEARLS

- Initial dose after eGFR ≥ 25 to < 60 mL/min/1.73m²: 10 mg daily (wait 4 weeks after initiation of SGLT2i and ensure eGFR stable)
- Order **SCr and lytes in 4 weeks** after **initiation, re-start or dose titration,** then every 2-4 months
- May cause an eGFR dip 3-3.5 ml/min/1.73m² over first 4 months of treatment (reflects kidney protection)
- Dosage adjustments based on K+:
  - If **K+ ≤ 4.8:** May ↑ to 20 mg daily if eGFR has not ↓ > 30% compared to prior measurement
  - If **K+ 4.8 – 5.5:** Maintain dose (consider K+ trends)
  - If **K+ ≥ 5.5:** Stop finerenone. Consider restarting at a lower dose when K+ ≤ 5.0 mmol/L and if tolerated without increased K+.
- Stop if eGFR not stable
- Remeasure K+ as needed based on patient characteristics and K+ levels and trends
- ⚠**AVOID** if on another MRA (spironolactone, eplerenone)
- ⚠**AVOID** if CHF NYHA Class II-IV present
- ⚠**AVOID** grapefruit (↑ serum concentration of finerenone)
- ⚠**AVOID** other strong CYP3A4 inhibitors (e.g., ketoconazole, ritonavir, clarithromycin)
- ⚠**RISKS:** Hyperkalemia, hypotension (rare, mean ↓ 3 mmHg)

COVERAGE

Nova Scotia Formulary: https://novascotia.ca/dhw/pharmacare/formulary.asp
Exception Status Drug Request Form: https://novascotia.ca/dhw/pharmacare/documents/forms/Standard-Exception-Status-Drug-Request-Form.pdf

Drug Class	Coverage	Notes
ACEi or ARB	BF	All drugs/strengths EXCEPT candesartan 4 mg.
SGLT2i	SFD (dapagliflozin); Exception status (canagliflozin, empagliflozin)	Exclusion criteria (Dapa and Empa): Treatment of T2D when glycemic control has not been achieved with metformin + SU or insulin is not an option OR (Empa) adjunctive treatment to diet, exercise, and standard care therapy to CV death in T2D and CVD when glycemic control has not been achieved with metformin.
MRA (finerenone)	Exception status	Criteria: Treatment of CKD and T2D with eGFR ≥ 25 mL/min/1.73m² and albuminuria ≥ 3 mg/mmol. Must be prescribed in consultation with a nephrologist. Excluded: CHF NYHA Class II-IV OR MRA. Discontinuation: eGFR < 15 mL/min/1.73m² or UACR ↑ from baseline
GLP-1RA (semaglutide)	Exception status	For the treatment of type 2 diabetes in combination with metformin and a sulfonylurea, when diet and exercise plus dual therapy with metformin and a sulfonylurea do not achieve adequate glycemic control. Maximum: 1 prefilled pen every 4 weeks

SICK DAY MEDICATION GUIDANCE

ADVISE PATIENTS...

TO STOP certain medications (**SADMANS**) when they are **unwell** (unable to keep food or fluid down) to reduce the risk of AKI
TO RE-START when symptoms have resolved and they have returned to normal eating and drinking

TRIGGERS FOR SDMG

- Vomiting
- Diarrhea
- Low Appetite
- Nausea
- New lightheadedness or weakness
- Lower weight or urine output
- Increased thirst

SADMANS

- Sulfonylureas, other secretagogues
- ACEi
- Diuretics, direct renin inhibitor
- Metformin
- ARB
- NSAIDs
- SGLT2i

Abbreviations: ACEi = angiotensin-converting enzyme inhibitor; AKI = acute kidney injury; ARB = angiotensin receptor blocker; BP = blood pressure; CHF = congestive heart failure; CKD = chronic kidney disease; CV = cardiovascular; D = Diabetes Assistance Program; DKA = diabetic ketoacidosis; eGFR = estimated glomerular filtration rate; GI = gastrointestinal; K^+ = potassium; MACE = major adverse cardiovascular events; MRA = mineralocorticoid receptor antagonists; NYHA = New York Heart Association; NSAID = non-steroidal anti-inflammatory drug; RAS = renin-angiotensin system; SCr = serum creatinine; SDMG = sick day medication guidance; SGLT2i = sodium-glucose cotransporter 2 inhibitor; SU = sulfonylurea; subcut = subcutaneous; T2D = type 2 diabetes; urine ACR = urine albumin-to-creatinine ratio

Summary

EARLY DETECTION

Screen individuals with T2D

eGFR **&** UACR

OPTIMIZE

Guideline-directed pillars for DKD

Questions or Comments

Please Fill Out an Evaluation Form

https://forms.office.com/r/TPY2DsB1v5