

📺 New #Tweertorial Drop! 📺

1/ Hey #NephTwitter! 🙋

We're back with a fresh #XTorial from @KIReports, this time diving into:

Dapagliflozin in Stage 4 CKD: no diabetes required? 😞

Let's unpack what this trial means for your next CKD patient. 💊💭

2/ Our #Tweertorial author is Stephanie @stephanietr612, adult nephrologist from @UTSWNephrology - No COI

[#MedTwitter](#) [#nephtwitter](#) [@ISNkidneycare](#) [#XTwitter](#)



3/

🗳️ Poll for nephrology folks:

Would you start an SGLT2 inhibitor in a patient with stage 4 CKD (eGFR <30) who does NOT have diabetes?

Yes, renal protection matters

No, too advanced

Only if diabetic

Only if proteinuric

Let's see what the ADAPT trial found 🙋

4/

🌟 ADAPT trial:

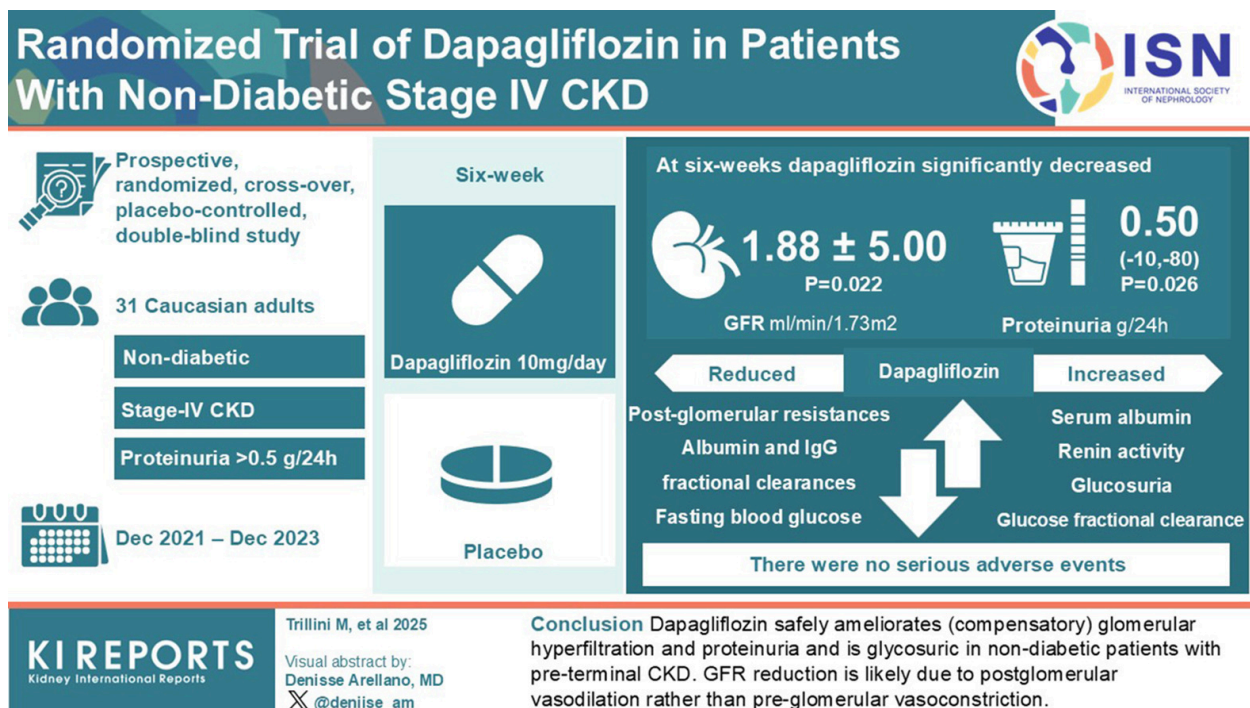
Trillini M et al., 2025. Randomized Trial of Dapagliflozin in Patients With Nondiabetic Stage 4 CKD

Does renal protection persist without diabetes?

✅ Yes: and the findings reshape the boundaries of SGLT2 benefit

🔗 [https://www.kireports.org/article/S2468-0249\(25\)00464-4/fulltext](https://www.kireports.org/article/S2468-0249(25)00464-4/fulltext)

VA @deniise_am



5/ 📖 Intro

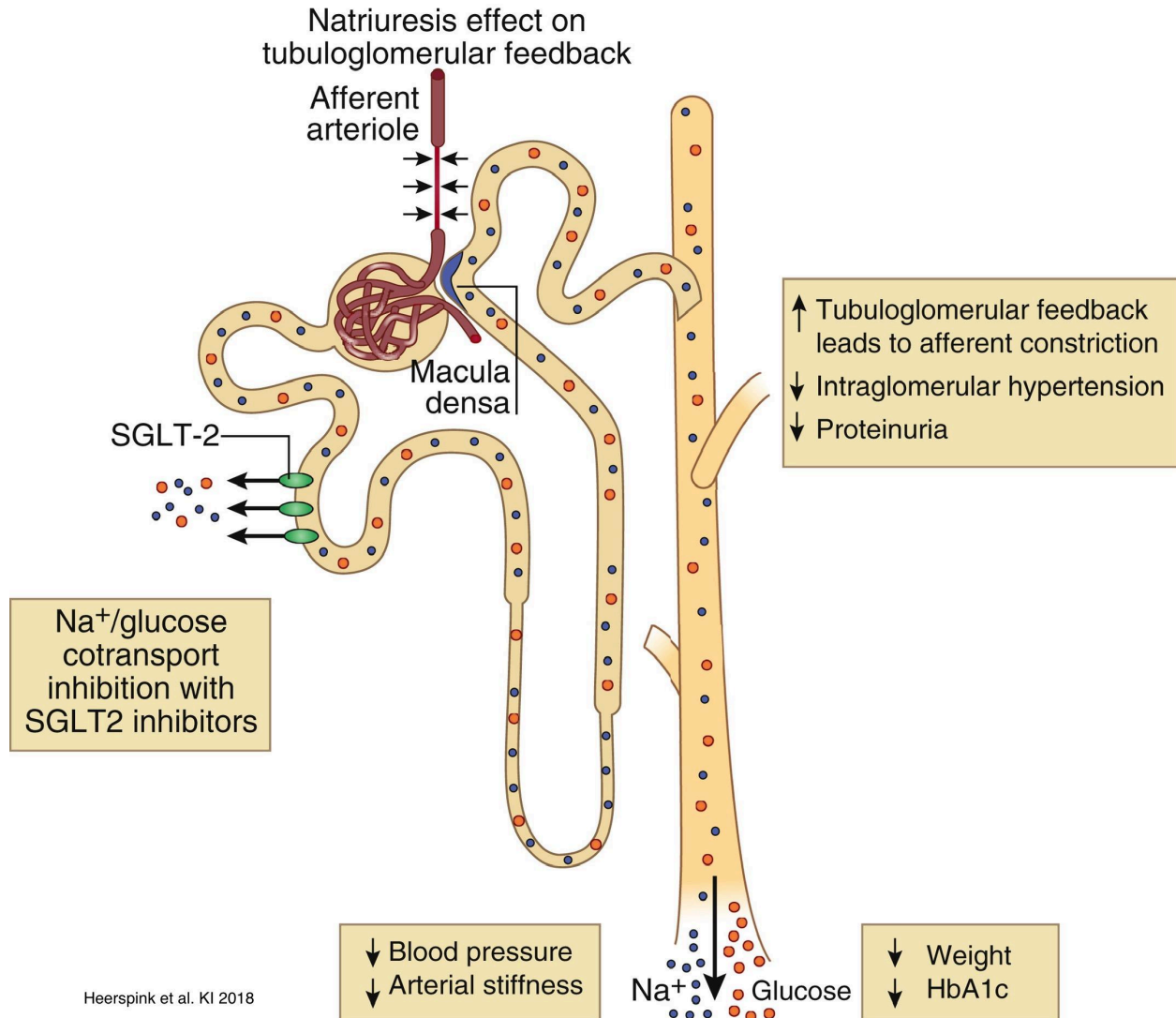
🍷 CKD = a major global health problem

Once considered an “orphan disease,” CKD care changed forever in 1982 when captopril became the first RAS inhibitor approved.

For decades, RAS blockade was our ONLY disease modifying therapy. ⌚

6/ Intro

⚡ SGLT2 inhibitors, first made for glucose control, surprised us with strong renal + CV protection (dapagliflozin, empagliflozin, canagliflozin). ✨ Their small, reversible eGFR dip (like RASi) hinted at the mechanism: more Na^+ to the macula densa \rightarrow restored tubuloglomerular feedback \rightarrow \downarrow glomerular pressure \rightarrow nephroprotection. 🧬



7/ Intro

🔍 So what's next?

If one way SGLT2i protect kidneys is through hemodynamic effects; can they do it even without diabetes and in advanced CKD (eGFR <30)?


That's exactly what the ADAPT trial set out to test. 🧪

8/ Methods

- Randomized, double-blind, placebo-controlled, cross-over

It tested dapagliflozin 10 mg vs placebo in nondiabetic stage 4 CKD with residual proteinuria despite optimized therapy.

9/ Methods

 Who was included?

Adults with:

- eGFR 15–30 mL/min/1.73m² (stable)
- Proteinuria >0.5 g/24h
- Controlled BP (<150/90 mmHg)

All on stable RAS blockade when possible.

Excluded: diabetes, pregnancy, or recent med changes

10/ Methods

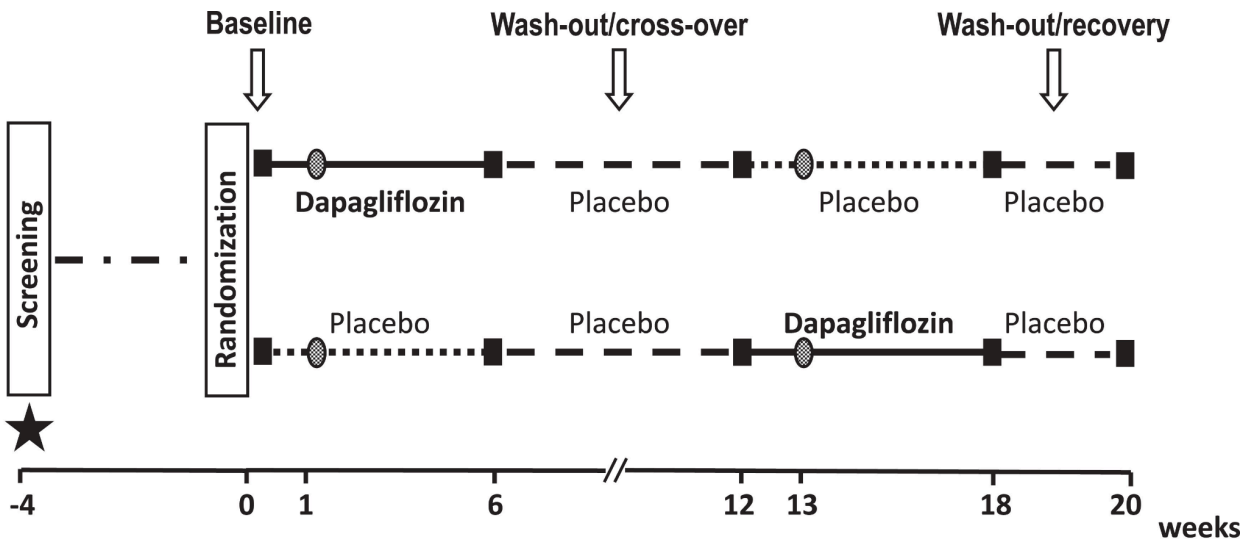
 **Crossover design:**

Patients received:

① 6 wks dapagliflozin → washout → 6 wks placebo

or

② 6 wks placebo → washout → 6 wks dapagliflozin



- ★ 24-hour urinary protein excretion (two consecutive evaluations >1 week apart during screening), blood glucose and HbA1C, creatinine and blood pressure
- Glomerular Filtration Rate (GFR) and Renal Plasma Flow (RPF) calculated by Iohexol and para-aminohippuric acid plasma clearance measurements, OGGT, 24 h urinary protein excretion and routine laboratory evaluations
- GFR and RPF calculated by Iohexol and para-aminohippuric acid plasma clearance measurements and routine laboratory evaluations

11/ ⚙️ Methods

Co-primary outcomes:

- ◆ Change in measured GFR (Iohexol)
- ◆ Change in 24-hr proteinuria after 6 wks of dapagliflozin vs placebo.

Secondary outcomes: systemic hemodynamics, renal vascular parameters, metabolic & safety measures

12/ 📊 Results

👤 Baseline (n=31):

- Mean GFR ~25 mL/min/1.73 m²
- Median proteinuria 1.8 g/day


- 90% on ACEi or ARB

Table 1. Baseline parameters of all randomized patients considered as a whole (overall) and according to the randomization to the 2 sequences of treatment with dapagliflozin followed by placebo or with placebo followed by dapagliflozin

Parameters	Overall N = 31	Dapagliflozin-placebo n = 15	Placebo- dapagliflozin n = 16	P-value ^a
Demographic parameters				
Age (yrs)	59.81 ± 14.87	57.87 ± 15.44	61.63 ± 14.59	0.491
Male sex, n (%)	26 (83.87)	12 (80.0)	14 (87.50)	0.654
Caucasian, n (%)	31 (100)	15 (100.0)	16 (100.0)	-
Current smoker, n (%)	6 (19.35)	2 (13.33)	4 (25.0)	0.654
Clinical parameters				
Body-mass index (kg/m ²)	26.06 ± 3.60	25.25 ± 3.61	26.82 ± 3.53	0.231
Systolic BP (mm Hg)	132.74 ± 9.59	129.27 ± 9.03	135.98 ± 9.19	0.050
Diastolic BP (mm Hg)	80.24 ± 7.13	78.74 ± 7.45	81.64 ± 6.75	0.264
Mean BP (mm Hg)	97.75 ± 7.21	95.58 ± 7.21	99.78 ± 6.81	0.106
Laboratory parameters				
Sodium (mEq/dl)	139.44 ± 2.33	139.77 ± 2.39	139.13 ± 2.31	0.453
Potassium (mEq/dl)	4.54 ± 0.49	4.58 ± 0.64	4.51 ± 0.31	0.713
Glucose (mg/dl)	97.90 ± 10.12	98.33 ± 12.34	97.50 ± 7.89	0.823
HbA1c (mmol/mol)	38.20 ± 4.39	38.68 ± 4.46	37.75 ± 4.42	0.564
Total serum protein (g/dl)	6.45 ± 0.32	6.48 ± 0.31	6.42 ± 0.33	0.599
Serum albumin (g/dl)	3.77 ± 0.33	3.82 ± 0.31	3.73 ± 0.35	0.459
Total cholesterol (mg/dl)	186.52 ± 38.44	184.87 ± 32.88	188.06 ± 44.06	0.821
Serum active renin (μU/ml)	50.5 (10.9–76.8)	19.3 (7.6–63.8)	56.4 (14.1–91.0)	0.304
Urine parameters				
Proteins (g/24 h)	1.80 (1.30–2.7)]	1.60 (1.00–2.70)	1.85 (1.40–3.25)	0.423
Albumin (μg/min)	820 (620–1260)	727 (540–1260)	844 (691–1510)	0.447
Glucose (mg/24 h)	301.5 ± 472.7	153.1 ± 71.7	461.2 ± 652.0	0.115
Sodium (mEq/24 h)	157.4 ± 55.3	149.4 ± 54.0	164.8 ± 57.1	0.446
Protein fractional clearance (× 10 ⁻⁵)	78.1 (47.4–122.7)	82.9 (40.6–122.7)	74.9 (55.7–143.9)	0.571
Albumin fractional clearance (× 10 ⁻⁵)	86.4 (56.2–152.1)	82.6 (42.3–152.1)	88.3 (59.6–150.9)	0.597
Glucose fractional clearance (× 10 ⁻⁵)	461 (304–774)	394 (304–511)	659 (371–1265)	0.164
Kidney function parameters				
Serum creatinine (mg/dl)	3.02 ± 0.60	3.03 ± 0.62	3.01 ± 0.59	0.942
GFR (ml/min per 1.73 m ²)	24.83 ± 5.04	24.78 ± 5.35	24.88 ± 4.90	0.955
CKD-EPI (ml/min per 1.73 m ²)	21.42 ± 4.71	21.33 ± 4.31	21.51 ± 5.19	0.921
MDRD (ml/min per 1.73 m ²)	22.62 ± 4.52	22.36 ± 4.07	22.86 ± 5.02	0.766
RPF (ml/min per 1.73 m ²)	324.68 ± 77.10	328.08 ± 100.20	321.70 ± 52.64	0.833
Glomerular resistances Ra (dyn·s/cm ⁵)	9660 ± 2375	9333 ± 2549	9946 ± 2256	0.491
Glomerular resistances Re (dyn·s/cm ⁵)	889.5 ± 176.8	891.4 ± 216.6	887.8 ± 140.6	0.957

BP, blood pressure; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; GFR, glomerular filtration rate; HbA1c, glycated hemoglobin; MDRD, Modification of Diet in Renal Disease; RPF, renal plasma flow.
^aPaired t test and Wilcoxon signed-rank test used for normally and non-normally distributed variables as necessary to calculate Δ dapagliflozin-placebo versus placebo-dapagliflozin. Data are mean ± SD or median with interquartile range (square brackets) or numbers and percentages (round brackets). Chemistries are serum values unless stated otherwise. Conversion factors for units: creatinine in mg/dl to μmol/l, × 88.4; cholesterol (total) in mg/dl to mmol/l, × 0.02586.

13/

 Results (6 weeks difference between dapagliflozin vs placebo):

- GFR ↓ 1.88 ± 5.00 mL/min/1.73 m² (p=0.022)
- Proteinuria ↓ 0.5 g/day (p=0.026)
- Effects seen by week 1 & fully reversed after withdrawal → functional, not injury.

14/[Poll]

 Pop quiz:

That early GFR dip after starting SGLT2i means:

Kidney damage
Glomerular hemodynamic reset

Keep reading 🖱️

15/✅ Glomerular hemodynamic reset

Common belief: ⬆️ pre-glomerular resistance ⬇️ GFR & RPF
But ADAPT found 📷: ⬇️ post-glomerular resistance ⬇️ GFR & RPF

Similar findings in patients with DM2, no CKD and no proteinuria (van Bommel et al, KI 2020)

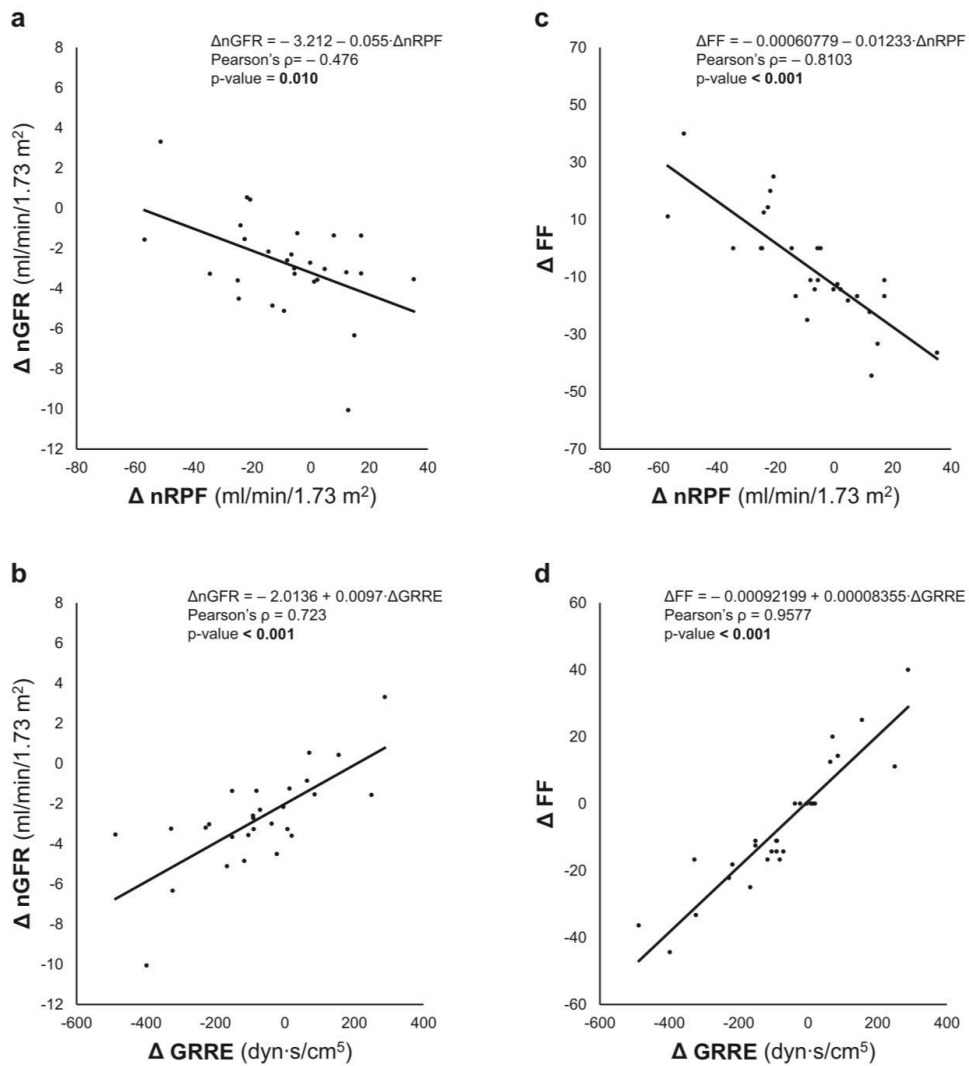



Figure 6. Linear regression model and Pearson correlation coefficient between changes in normalized GFR (or filtration fraction [FF]) and corresponding changes in (a and c) normalized renal plasma flow (RPF), and (b and d) efferent glomerular vascular resistance (GRRE) during the dapagliflozin treatment period. GFR, glomerular filtration rate.

16/

 Secondary findings:

 Filtration fraction

 Serum albumin

 Renin (RAS synergy)

 Glucosuria even with eGFR <30

No serious adverse events 🙌

17/⚖️ Limitations & Strengths

❌ Small, single-center pilot with short follow-up ⌚ limits generalizability, esp. since 11/31 were on dual RAS blockade (not common practice)

💪 But ✅ gold-standard GFR/RPF measures, crossover design, and high retention strengthen the data quality = good for mechanistic and safety study

18/👉 Proposed clinical meaning:

In patients with advanced CKD & no diabetes, dapagliflozin:

✅ Lowers proteinuria

✅ Normalizes glomerular hemodynamics

✅ Is safe & reversible

⚠️ However, studies about further contributory mechanisms and studies with longer follow-up are needed

19/

💬 So back to our initial poll...

Would you start dapagliflozin in stage 4 CKD without diabetes, now that you've seen ADAPT's data?

👉 Share your thoughts & tag a nephrology friend